Organocatalytic Enantioselective Functionalization of Indoles in the Carbocyclic Ring with Cyclic Imines

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SUPPORTING INFORMATION

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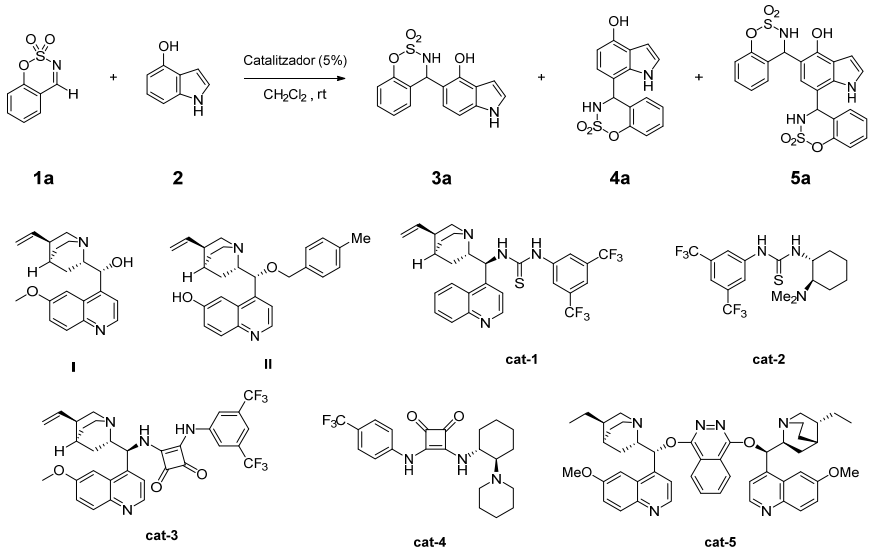
General Experimental Methods

Dicloromethane, 1,2-dichloroethane and toluene were distilled from CaH_2. Tetrahydrofuran (THF) and Et_2O were distilled from sodium benzophenone ketyl. Reactions were monitored by TLC (thin layer chromatography) analysis using Merck Silica Gel 60 F-254 thin layer plates. Flash column chromatography was performed on Merck silica gel 60, 0.040–0.063 mm. Melting points were determined in capillary tubes. NMR spectra were run in a Bruker DPX300 spectrometer (Bruker, Billerica, MA, USA) at 300 MHz for ^{1}H and at 75 MHz for ^{13}C using residual non-deuterated solvent as internal standard ($CHCl_3$: δ 7.26 for ^{1}H and 77.0 ppm for ^{13}C; DMSO-d6 δ 2.50 for ^{1}H and 39.52 ppm for ^{13}C). Chemical shifts are given in ppm. The carbon type was determined by DEPT (Distortionless Enhancement by Polarization Transfer) experiments. High resolution mass spectra (ESI) were recorded on a TRIPLETO^{FT}5600 spectrometer LC/MS/MS System, (AB SCIEX) equipped with Ion Spray Voltage (ISVF): 5500. The MS was using method with infusion experiment. Data was evaluated using the PeakView™ . Specific optical rotations were measured using sodium light (D line 589 nm). Chiral HPLC (High performance liquid chromatography) analyses were performed in a chromatograph equipped with a UV diode-array detector using chiral stationary columns from Daicel. Benzoxathiazine 2,2-dioxides were prepared as described in the literature.[1] 4-Hydroxyindole **2** and 5-Hydroxyindole **6** were purchased from Apollo Scientific. 6-Hydroxyindole **8** was purchased from Fluorochem. 7-Hydroxyindole **13** was purchased from Flurochem and purified by column chromatography (hexanes:EtOAc). Catalyts **II**-**XII** were prepared from quinine following the methodology reported by Deng.[2]

Catalyst screening for the enantioselective aza-Friedel-Crafts reaction

Table S1: Optimization of the organocatalyst.



Entry	Catalyst	Time	3a		4a	5a	
			Yield (%)	e.e. (%)	Yield (%)	Yield (%)	d.r.
1	**I**	21 h	48	Rac.	6	34	50:50
2	**II**	24 h	57	33	9	28	52:48
3	**Cat-1**	17 h	75	Rac.	2	6	43:57
4	**Cat-2**	6 h	81	7	2	17	54:46
5	**Cat-3**	16 h	93	5	2	4	55:45
6	**Cat-4**	17 h	84	Rac.	2	14	53:47
7	**Cat-5**	16 h	21	5	No det.	No det.	Not det.

General procedure for the non-enantioselective *aza*-Friedel-Crafts reaction

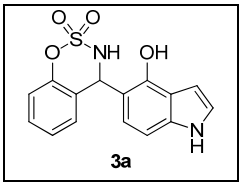
In a 5 mL vial, hydroxyindole (0,2 mmol, 2 eq.), cyclic imine **1** (0,1 mmol, 1 eq.), (3,5-bis(trifluoromethyl)phenyl)-3-(2-(dimethylamino)ethyl) thiourea (3 mg, 0.02 mmol, 0.2 eq) and a stir bar were placed, and were dissolved in CH_2Cl_2 (1 mL). The mixture was stirred at room temperature until completion (TLC). Finally, the reaction mixture was directly poured into a column for chromatography, using hexane:EtOAc as eluent to afford the Friedel-Crafts products.

General procedure for the enantioselective aza-Friedel-Crafts reaction

In a 5 mL vial, hydroxyindole (0,2 mmol, 2 eq.), cyclic imine 1 (0,1 mmol, 1 eq.), organocatalyst XII (2 mol%) and a stir bar were placed, and were dissolved in $ClCH_2CH_2Cl$ (1 mL). The mixture was stirred at room temperature until completion (TLC). Finally, the reaction mixture was directly poured into a column for chromatography, using hexane:EtOAc as eluent to afford the Friedel-Crafts products.

Characterization of compounds 3

4-(4-Hydroxy-1H-indol-5-yl)-3,4-dihydrobenzo[e][1,2,3]oxathiazine 2,2-dioxide (3a)

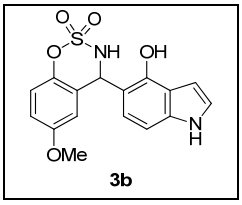


3a

Enantiomeric excess (67%) was determined by chiral HPLC (Chiralcel OD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer rt = 16.4 min, minor enantiomer rt = 40.7 min.

White solid, decompose >200 ºC; $[\alpha]_{20}^{D}$= +21.1 (c=0.74, MeOH) (67% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.26 (dddd, *J* = 8.2, 7.3, 1.6, 0.8 Hz, 1H), 7.10 (d, *J* = 8.4 Hz, 1H), 7.08 – 7.02 (m, 2H), 6.98 (td, *J* = 7.6, 1.2 Hz, 1H), 6.79 – 6.74 (m, 1H), 6.48 (ddd, *J* = 3.3, 2.0, 0.7 Hz, 1H), 6.04 (d, *J* = 9.8 Hz, 1H), 5.63 (d, *J* = 9.8 Hz, 1H), 5.27 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) 151.08 (C), 146.66 (C), 137.94 (C), 129.18 (CH), 127.56 (CH), 124.94 (CH), 124.92 (CH), 124.45 (CH), 123.42 (C), 118.32 (CH), 118.15 (C), 112.73 (C), 104.82 (CH), 97.96 (CH), 59.96 (CH). HRMS (ESI) m/z: 317.0580 $[M + H]^+$, $C_{15}H_{13}N_2O_4S$ required 317.0591.

4-(4-Hydroxy-1H-indol-5-yl)-6-methoxy-3,4-dihydrobenzo[e][1,2,3]oxathiazine 2,2-dioxide (3b)

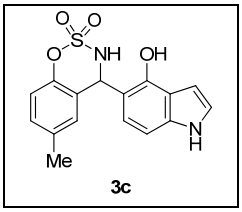


3b

Enantiomeric excess (5%) was determined by chiral HPLC (Chiralcel OD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer rt = 19.9 min, minor enantiomer rt = 48.6 min.

White solid, m.p. = 127-129 ºC; $[\alpha]_{20}^{D}$= +0.41 (c=0.735, MeOH) (5% *ee*); ^{1}H NMR(300 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.20 (dd, *J* = 3.4, 2.4 Hz, 1H), 7.08 (d, *J* = 8.4 Hz, 1H), 7.05 (dd, *J* = 8.3, 0.8 Hz, 1H), 6.98 (d, *J* = 9.0 Hz, 1H), 6.78 (ddd, *J* = 9.0, 3.0, 0.8 Hz, 1H), 6.48 (ddd, *J* = 3.3, 2.1, 0.7 Hz, 1H), 6.28 (dd, *J* = 3.0, 1.0 Hz, 1H), 6.00 (d, *J* = 9.7 Hz, 1H), 5.55 (d, *J* = 9.8 Hz, 1H), 5.34 (s, 1H), 3.58 (s, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 156.38 (C), 146.77 (C), 144.93 (C), 137.97 (C), 124.73 (CH), 124.39 (C), 124.36 (CH), 119.09 (CH), 118.18 (C), 114.18 (CH), 112.74 (CH), 112.54 (C), 104.77 (CH), 98.13 (CH), 59.97 (CH), 55.56 (CH_3). HRMS (ESI) m/z: 346.0686 $[M + H]^+$, $C_{16}H_{15}N_2O_5S$ required 346.0696.

4-(4-Hydroxy-1H-indol-5-yl)-6-methyl-3,4-dihydrobenzo[e][1,2,3]oxathiazine 2,2-dioxide (3c)

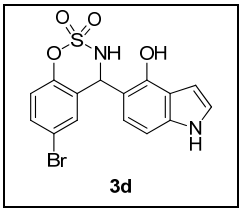


3c

Enantiomeric excess (50%) was determined by chiral HPLC (Chiralcel OD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer rt = 15.15 min, minor enantiomer rt = 41.7 min.

White solid, decompose >180 ºC; $[\alpha]_{20}^{D}$= +7.30 (c=0.98, MeOH) (50% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.20 (dd, J = 3.4, 2.4 Hz, 1H), 7.10 – 7.02 (m, 3H), 6.93 (d, J = 8.4 Hz, 1H), 6.58 – 6.53 (m, 1H), 6.50 (dd, J = 3.2, 2.2 Hz, 1H), 6.00 (d, J = 9.7 Hz, 1H), 5.55 (d, J = 9.6 Hz, 1H), 5.28 (s, 1H), 2.12 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.01 (C), 146.69 (C), 137.92(C), 134.74 (C), 129.86 (CH), 127.69 (CH), 124.93 (CH), 124.40 (CH), 122.87 (C), 118.18 (C), 118.11 (CH), 112.85 (C), 104.83 (CH), 98.05 (CH), 59.89 (CH), 20.72 (CH_3). HRMS (ESI) m/z: 331.0748 $[M + H]^+$, $C_{16}H_{15}N_2O_4S$ required 331.0747.

6-Bromo-4-(4-hydroxy-1H-indol-5-yl)-3,4-dihydrobenzo[e][1,2,3]oxathiazine 2,2-dioxide (3d)



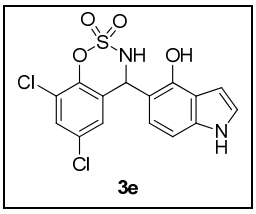
3d

Enantiomeric excess (70%) was determined by chiral HPLC (Chiralcel OD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer rt = 14.1 min, minor enantiomer rt = 44.6 min.

White solid, decompose >140 ºC; $[\alpha]_{20}^{D}$= -13,39 (c=1,18, MeOH) (70% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.35 (s, 1H), 7.36 (ddd, *J* = 8.7, 2.4, 0.9 Hz, 1H), 7.24 – 7.21 (m, 1H), 7.09 (s, 2H), 6.93 (d, *J* = 8.7 Hz, 1H), 6.88 (dd, *J* = 2.4, 1.0 Hz, 1H), 6.49 (dd, *J* = 3.3, 2.1 Hz, 1H), 5.98 (d, *J* = 10.0 Hz, 1H), 5.67 (d, *J* = 9.3 Hz, 1H), 5.31 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.11 (C), 146.57 (C), 138.10 (C), 132.17 (CH), 130.19 (CH), 125.61 (C),

124.80 (CH), 124.59 (CH), 120.03 (CH), 118.12 (C), 117.66 (C), 111.89 (C), 105.06 (CH), 97.97 (CH), 59.81 (CH). HRMS (ESI) m/z: 394.9693 $[M + H]^+$, $C_{15}H_{12}N_2O_4SBr$ required 394.9696.

6,8-Dichloro-4-(4-hydroxy-1H-indol-5-yl)-3,4-dihydrobenzo[e][1,2,3]oxathiazine 2,2-dioxide (3e)



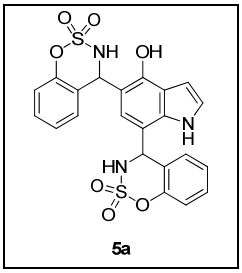
3e

Enantiomeric excess (67%) was determined by chiral HPLC (Chiralcel OD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer rt = 15.2 min, minor enantiomer rt = 41.7 min.

White solid, decompose >185 ºC; $[\alpha]_{20}^{D}$= +23.55 (c=1.087, MeOH) (67% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$/MeOD) δ 7.15 (dd, *J* = 2.5, 0.9 Hz, 1H), 6.99 (d, *J* = 3.3 Hz, 1H), 6.85 (dd, *J* = 8.3, 0.8 Hz, 1H), 6.80 (d, *J* = 8.4 Hz, 1H), 6.53 (dd, *J* = 2.5, 1.1 Hz, 1H), 6.48 (dd, *J* = 3.3, 0.8 Hz, 1H), 5.86 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.77 (C), 145.55 (C), 138.22 (C), 129.16 (C), 128.80 (CH), 127.36 (C), 125.89 (CH), 123.75 (CH), 123.45 (C), 123.36 (CH), 118.11 (C), 110.78 (C), 103.87 (CH), 98.38 (CH), 58.96 (CH). HRMS (ESI) m/z: 384.3812 $[M + H]^+$, $C_{15}H_{11}Cl_2N_2O_4S$ required 384.9811.

Characterization of compounds 5a

4,4'-(4-Hydroxy-1*H*-indole-5,7-diyl)bis(3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide) (5a)

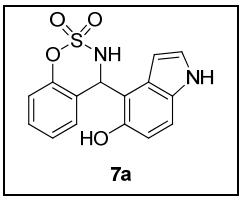


5a

Brown solid, decompose > 150 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.70 (s, 1H), 8.64 (s, 1H), 7.42 – 7.34 (m, 2H), 7.33 – 7.25 (m, 2H), 7.21 – 6.88 (m, 15H), 6.77 (dd, *J* = 3.0, 1.2 Hz, 1H), 6.75 (dd, *J* = 3.0, 1.4 Hz, 1H), 6.55 (dd, *J* = 3.3, 2.0 Hz, 1H), 6.52 (dd, *J* = 3.3, 2.0 Hz, 1H), 6.22 – 6.12 (m, 2H), 6.01 (m, 2H), 5.77 (s, 1H), 5.69 (d, *J* = 9.8 Hz, 1H), 5.60 (d, *J* = 9.6 Hz, 1H), 5.10 (d, *J* = 6.7 Hz, 1H), 5.05 (d, *J* = 7.2 Hz, 1H). HRMS (ESI) m/z: 500.0581$[M + H]^+$, $C_{15}H_{11}Cl_2N_2O_4S$ required 500.0581.

Characterization of compounds 7

4-(5-Hydroxy-1H-indol-4-yl)-3,4-dihydrobenzo[e][1,2,3]oxathiazine 2,2-dioxide (7a)

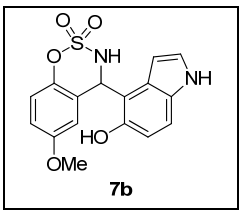


7a

Enantiomeric excess (80%) was determined by chiral HPLC (Chiralcel OD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer rt = 11.3 min, minor enantiomer rt = 13.8 min.

White solid, decompose >202 ºC; $[\alpha]_{20}^{D}$= +89.77 (c=1.10, MeOH) (80% *ee*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 ºC) δ 10.81 (s, 1H), 9.08 (s, 1H), 8.20 (s, 1H), 7.33 – 7.26 (m, 2H), 7.15 (s, 1H), 7.12 (dd, J = 8.3, 1.0 Hz, 1H), 7.02 (td, J = 7.7, 1.1 Hz, 1H), 6.79 (d, J = 8.6 Hz, 1H), 6.71 (d, J = 7.8 Hz, 1H), 6.45 (s, 1H), 5.96 (s, 1H). ^{13}C NMR (125 MHz, DMSO-d_6, 60 ºC) δ 150.56 (C), 148.28 (C), 130.70 (C), 128.43 (CH), 127.31 (CH), 126.82 (C), 125.40 (CH), 124.62 (CH), 123.54 (C), 117.55 (CH), 112.50 (CH), 111.98 (C), 111.24 (CH), 99.53 (CH), 54.15 (CH). HRMS (ESI) m/z: 317.0595 $[M + H]^+$, $C_{15}H_{13}N_2O_4S$ required 317.0591.

4-(5-Hydroxy-1H-indol-4-yl)-6-methoxy-3,4-dihydrobenzo[e][1,2,3]oxathiazine 2,2-dioxide (7b)



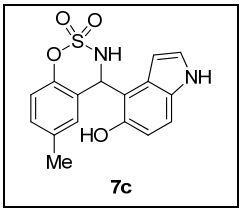
7b

Enantiomeric excess (85%) was determined by chiral HPLC (Chiralcel OD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer rt = 12.4 min, minor enantiomer rt = 16.5 min.

White solid, decompose >180 ºC $[\alpha]_{20}^{D}$= 50.79 (c=0.75, MeOH) (85% *ee*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 ºC) δ 10.82 (s, 1H), 9.09 (s, 1H), 8.07 (s, 1H), 7.28 (dd, *J* = 8.6, 0.8 Hz, 1H), 7.17 (s, 1H), 7.09 (d, *J* = 9.0 Hz, 1H), 6.89 (ddd, *J* = 9.0, 3.0, 0.6 Hz, 1H), 6.79 (d, *J* = 8.6 Hz, 1H), 6.39 (s, 1H), 6.20 (dd, *J* = 3.0, 0.9 Hz, 1H), 6.01 (s, 1H), 3.53 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6, 60 ºC) δ 155.76 (C), 148.18 (C), 144.40 (C), 130.69 (C), 126.77 (C), 125.47 (CH), 124.56 (C), 118.48 (CH), 113.38 (CH), 112.67 (CH), 112.53 (CH), 112.02 (C),

111.25 (CH), 99.50 (CH), 55.18 (CH_3), 54.21 (CH). HRMS (ESI) m/z: 347.0694 $[M + H]^+$, $C_{16}H_{15}N_2O_5S$ required 347.0696.

4-(5-Hydroxy-1*H*-indol-4-yl)-6-methyl-3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (7c)

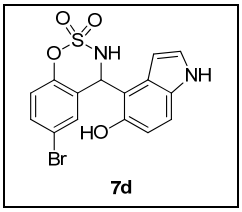


7c

Enantiomeric excess (85%) was determined by chiral HPLC (Chiralcel OD-H), hexane-iPrOH 90:10, 1.0 mL/min, major enantiomer rt = 38.7min, minor enantiomer rt = 58.6 min.

White solid, decompose >189 ºC $[\alpha]_{20}^{D}$= 53.73 (c=1.04, MeOH) (85% *ee*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 ºC) δ 10.81 (s, 1H), 9.07 (s, 1H), 8.06 (s, 1H), 7.28 (dd, *J* = 8.6, 0.8 Hz, 1H), 7.16 (s, 1H), 7.12 – 7.07 (m, 1H), 7.02 (d, *J* = 8.3 Hz, 1H), 6.79 (d, *J* = 8.6 Hz, 1H), 6.52 (d, *J* = 1.0 Hz, 1H), 6.40 (s, 1H), 5.99 (d, *J* = 4.2 Hz, 1H), 2.07 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6, 60 ºC) δ 149.48 (C), 149.14 (C), 134.70 (C), 131.64 (C), 129.92 (CH), 128.14 (CH), 127.80 (C), 126.37 (CH), 124.15 (C), 118.38 (CH), 113.43 (CH), 113.06 (C), 112.22 (CH), 100.49 (CH), 55.06 (CH), 20.89 (CH_3).HRMS (ESI) m/z: 331.0749 $[M + H]^+$, $C_{16}H_{15}N_2O_4S$ required 331.0747.

6-Bromo-4-(5-hydroxy-1*H*-indol-4-yl)-3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (7d)

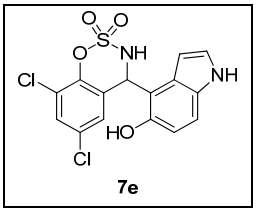


7d

Enantiomeric excess (84%) was determined by chiral HPLC (Chiralcel OD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer rt = 10.0 min, minor enantiomer rt = 13.5 min.

White solid, m.p. = 135-143 ºC $[\alpha]_{20}^{D}$= +19.09 (c=0.985, MeOH) (84% *ee*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 ºC) δ 10.89 (s, 1H), 9.15 (s, 1H), 8.38 (s, 1H), 7.49 (ddd, *J* = 8.8, 2.5, 0.8 Hz, 1H), 7.31 (dd, *J* = 8.6, 0.8 Hz, 1H), 7.20 (t, *J* = 2.5 Hz, 1H), 7.14 (d, *J* = 8.7 Hz, 1H), 6.80 (d, *J* = 8.6 Hz, 1H), 6.79 (dd, *J* = 2.4, 1.0 Hz, 1H), 6.43 (s, 1H), 6.01 (s, 1H) ^{13}C NMR (125 MHz, DMSO-d_6, 60 ºC) δ 149.91 (C), 148.36 (C), 131.36 (CH), 130.67 (C), 129.48 (CH), 126.70 (C), 126.01 (C), 125.72 (C), 120.06 (CH), 116.32 (C), 112.92 (CH), 111.31 (CH), 111.24 (C), 99.31 (CH), 53.96 (CH). HRMS (ESI) m/z: 394.9693 $[M + H]^+$, $C_{15}H_{12}BrN_2O_4S$ required 394.9696.

6,8-Dichloro-4-(5-hydroxy-1*H*-indol-4-yl)-3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (7e)

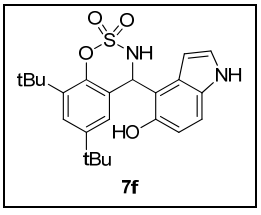


7e

Enantiomeric excess (86%) was determined by chiral HPLC (Chiralcel OD-H), hexane-iPrOH 90:10, 1.0 mL/min, major enantiomer rt = 28.9 min, minor enantiomer rt = 53.3 min.

White solid, decompose >160 ºC $[\alpha]_{20}^{D}$= 60.72 (c=0.97, MeOH) (86% *ee*); ^{1}H NMR (500 MHz, DMSO-$d_6$60 ºC) δ 10.91 (s, 1H), 9.17 (s, 1H), 8.74 (s, 1H), 7.66 (dd, *J* = 2.5, 0.5 Hz, 1H), 7.32 (dd, *J* = 8.6, 0.5 Hz, 1H), 7.22 (t, *J* = 2.7 Hz, 1H), 6.80 (d, *J* = 8.7 Hz, 1H), 6.63 (dd, *J* = 2.5, 0.9 Hz, 1H), 6.45 (s, 1H), 6.00 (s, 1H). ^{13}C NMR (125 MHz, DMSO-$d_6$60 ºC) δ 148.48 (C), 145.43 (C), 130.62 (C), 128.44 (CH), 128.34 (C), 127.23 (C), 126.66 (C), 125.88 (CH), 125.57 (CH), 122.62 (C), 113.15 (CH), 111.29 (CH), 110.73 (C), 99.15 (CH), 54.31 (CH). HRMS (ESI) m/z: 384.9810 $[M + H]^+$, $C_{15}H_{11}Cl_2N_2O_4S$ required 384.9811.

6,8-Di-*tert*-butyl-4-(5-hydroxy-1*H*-indol-4-yl)-3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (7f)



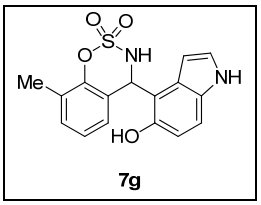
7f

Enantiomeric excess (82%) was determined by chiral HPLC (Chiralcel OD-H), hexane-iPrOH 90:10, 1.0 mL/min, major enantiomer rt = 15.1 min, minor enantiomer rt = 31.0 min.

White solid, decompose > 235 ºC $[\alpha]_{20}^{D}$= +54.54 (c=0.77, MeOH) (82% *ee*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 ºC) δ 10.75 (s, 1H), 9.05 (s, 1H), 8.04 (s, 1H), 7.26 (dd, *J* = 8.6, 0.9 Hz, 1H), 7.24 (dd, *J* = 2.4, 0.5 Hz, 1H), 7.15 (t, *J* = 2.7 Hz,

1H), 6.78 (d, *J* = 8.6 Hz, 1H), 6.68 (dd, *J* = 2.4, 0.9 Hz, 1H), 6.41 (s, 1H), 6.01 (s, 1H), 1.43 (s, 9H), 1.03 (s, 9H). ^{13}C NMR (125 MHz, DMSO-d_6, 60 ºC) δ 147.94 (C), 147.46 (C), 145.77 (C), 137.31 (C), 130.70 (C), 126.80 (C), 125.25 (CH), 123.55 (C), 122.16 (CH), 122.03 (CH), 112.86 (C), 112.23 (CH), 111.15 (CH), 99.53 (CH), 54.37 (CH), 34.30 (C), 33.71 (C), 30.62 (CH), 29.65 (CH). HRMS (ESI) m/z: 429.1825 $[M + H]^+$, $C_{23}H_{29}N_2O_4S$ required 429.1843.

4-(5-Hydroxy-1H-indol-4-yl)-8-methyl-3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (7g)

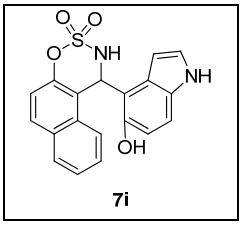


7g

Enantiomeric excess (81%) was determined by chiral HPLC (Chiralcel OD-H), hexane-iPrOH 90:10, 1.0 mL/min, major enantiomer rt = 37.9 min, minor enantiomer rt = 61.1 min.

White solid, decompose > 195 ºC $[\alpha]_{20}^{D}$= +89.06 (c=1.07, MeOH) (81% *ee*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 ºC) δ 10.80 (s, 1H), 9.06 (s, 1H), 8.13 (s, 1H), 7.27 (dd, *J* = 8.6, 0.5 Hz, 1H), 7.17 (dd, *J* = 7.4, 0.7 Hz, 1H), 7.14 (t, *J* = 2.5 Hz, 1H), 6.89 (t, *J* = 7.6 Hz, 1H), 6.78 (d, *J* = 8.6 Hz, 1H), 6.53 (d, *J* = 7.5 Hz, 1H), 6.42 (s, 1H), 5.98 (s, 1H), 2.27 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 148.99 (C), 148.18 (C), 130.69 (C), 129.60 (CH), 126.82 (C), 126.12 (C), 125.37 (CH), 124.84 (CH), 123.87 (CH), 123.34 (C), 112.39 (CH), 112.24 (C), 111.22 (CH), 99.58 (CH), 54.14 (CH), 30.28 (CH_3) .HRMS (ESI) m/z: 331.0748 $[M + H]^+$, $C_{16}H_{15}N_2O_4S$ required 331.0747.

1-(5-Hydroxy-1*H*-indol-4-yl)-1,2-dihydronaphtho[1,2-*e*][1,2,3]oxathiazine 3,3-dioxide (7h)



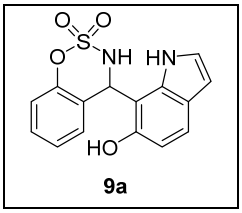
7i

Enantiomeric excess (38%) was determined by chiral HPLC (Chiralpack AD-H), hexane-iPrOH 90:10, 1.0 mL/min, major enantiomer rt = 21.2 min, minor enantiomer rt = 47.4 min.

White solid, decompose > 185 ºC $[\alpha]_{20}^{D}$= +13.09 (c=0.695, MeOH) (38% *ee*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 ºC) (presence of rotamers in 1:0,8* proportion) δ 10.64* (s, 1H), 10.55 (s, 1H), 8.04 (d, *J* = 9.0 Hz, 1H), 7.97* (d, *J* = 3.4 Hz, 1H), 7.95 (s, 1H), 7.87* (d, *J* = 8.0 Hz, 1H), 7.69* (d, *J* = 8.6 Hz, 1H), 7.62 (d, *J* = 8.6 Hz, 1H), 7.49 – 7.41 (m, 1H), 7.39 – 7.30** (m, 4H), 7.24* (t, *J* = 7.3 Hz, 1H), 7.19* (dd, *J* = 8.6, 0.7 Hz, 1H), 7.17 (d, *J* = 8.6 Hz, 1H), 6.95* (s, 1H), 6.92 (d, *J* = 2.1 Hz, 1H), 6.86 (s, 1H), 6.80* (d, *J* = 8.5 Hz, 1H), 6.68 – 6.64 (m, 2H), 6.51 (s, 1H), 5.64* (s, 1H). ^{13}C NMR (125 MHz, DMSO-d_6, 60 ºC) δ 150.45, 148.91, 148.88*, 147.45*, 130.78, 130.54, 130.50, 130.37, 130.17, 130.11, 129.94, 129.80, 128.24, 128.20*, 126.70, 126.41, 126.22, 125.94, 125.06, 124.97, 124.83, 123.67, 122.93, 118.02, 117.97, 117.30, 115.47, 113.66, 112.28, 111.77, 111.71, 111.53, 111.38, 111.01, 102.45, 98.85, 52.06. HRMS (ESI) m/z: 367.0746 $[M + H]^+$, $C_{19}H_{15}N_2O_4S$ required 367.0747.

<u>Characterization of compound 9</u>

4-(6-Hydroxy-1*H*-indol-7-yl)-3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (9a)



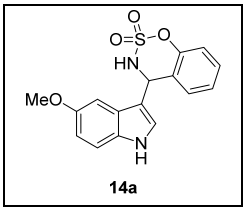
9a

Enantiomeric excess (38%) was determined by chiral HPLC (Chiralcel OD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer rt = 13.0 min, minor enantiomer rt = 10.1 min.

Oil; $[\alpha]_{20}^{D}$= +35.30 (c=0.12, $CHCl_3$) (37% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.50 (dd, *J* = 8.4, 0.5 Hz, 1H), 7.29 – 7.20 (m, 1H), 7.07 (dd, *J* = 3.1, 2.5 Hz, 1H), 7.01 (dd, *J* = 8.3, 1.0 Hz, 1H), 6.95 (tt, *J* = 7.5, 1.4 Hz, 1H), 6.74 – 6.65 (m, 1H), 6.62 (dd, *J* = 8.4, 0.7 Hz, 1H), 6.51 (dd, *J* = 3.3, 2.0 Hz, 1H), 6.35 (d, *J* = 9.0 Hz, 1H), 5.87 (d, *J* = 9.0 Hz, 1H), 5.28 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.96 (C), 149.40 (C), 135.21 (C), 129.56 (CH), 127.09 (CH), 125.47 (CH), 124.32 (CH), 123.43 (C), 122.45 (CH), 121.90 (C), 118.50 (CH), 110.28 (CH), 105.31 (C), 103.27 (CH), 54.82 (CH). HRMS (ESI) m/z: 317.0592 $[M + H]^+$, $C_{15}H_{13}N_2O_4S$ required 317.0591.

Characterization of compounds 11

4-(5-Methoxy-1*H*-indol-3-yl)-3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (11)



14a

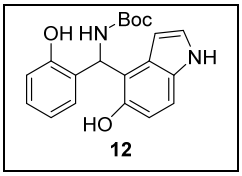
Enantiomeric excess (6%) was determined by chiral HPLC (Chiralcel IC), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer rt = 12.2 min, minor enantiomer rt = 24.2 min.

White solid, decompose > 157 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.69 (dd, *J* = 5.7, 3.3 Hz, 1H), 7.51 (dd, *J* = 5.7, 3.3 Hz, 1H), 7.31 (m, 2H), 7.24 (s, *J* = 1.5 Hz, 1H), 7.13 – 7.05 (m, 2H), 6.88 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.64 (d, *J* = 2.4 Hz, 1H), 6.23 (s, 1H), 3.70 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.63 (C), 151.30 (C), 131.58 (C), 129.65 (CH), 128.41 (CH), 125.45 (C), 125.33 (CH), 125.27 (CH), 121.74 (C), 118.79 (CH), 113.42 (CH), 112.59 (CH), 112.30 (C), 100.45 (CH), 55.75 (CH), 55.12 (CH). HRMS (ESI) m/z: 367.0746 $[M + H]^+$, $C_{19}H_{15}N_2O_4S$ required 367.0747.

Reaction procedure and characterization of compound 12.

Compound **7a** (0,072 mmol) was dissolved in a 10mL round bottom flask with dry THF (2 ml). After stirring 10 minutes, $LiAlH_4$ (0,21 ml, 1M, 0.216 mmol, 3 eq) was added dropwise. The reaction mixture was stirred at room temperature overnight. Then, the reaction mixture was quenched with EtOAc(1 mL), EtOH (1 mL) and H_2O (1 mL). To the resulting turbid mixture $(Boc)_2O$ (0,22 mmol) was added in one portion and the resulting mixture was stirred at rt for 1h. The mixture was diluted with EtOAc (15 mL) and NH_4Cl sat (15 mL). The aqueous layer was the separated and extracted with EtOAc (2 x 20 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, filtered and concentrated in vacuo, Purification of the residue by flash chromatography afforded compound **12**.

tert-Butyl ((5-hydroxy-1*H*-indol-4-yl)(2-hydroxyphenyl)methyl)carbamate (12)



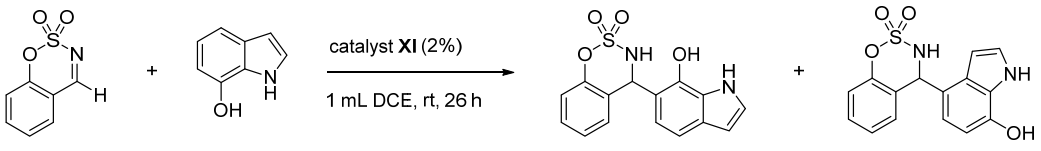
12

Enantiomeric excess (81%) was determined by chiral HPLC (Chiralcel AD-H), hexane-iPrOH 90:10, 1.0 mL/min, major enantiomer rt = 29.7 min, minor enantiomer rt = 34.2 min.

White solid, decompose > 150 ºC $[\alpha]_{20}^{D}$= 61.08 (c=1.015, MeOH) (81% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.88 (s, 1H), 8.11 (s, 1H), 7.26 – 7.19 (m, 1H), 7.15 (dd, *J* = 8.6, 0.9 Hz, 1H), 7.07 (m, 1H), 7.01 – 6.93 (m, 1H), 6.89 (dd, *J* = 8.1, 1.2 Hz, 1H), 6.80 – 6.69 (m, 2H), 6.54 (d, *J* = 8.3 Hz, 1H), 6.48 – 6.41 (m, 1H), 6.12 (s, 1H), 1.42 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.55 (C=O), 154.53 (C), 146.53 (C), 131.33 (C), 128.76 (CH), 127.95 (CH), 127.79 (C), 126.97 (C), 125.41 (CH), 120.06 (CH), 117.37 (CH), 115.78 (C), 113.07 (CH), 111.25 (CH), 100.74 (CH), 80.90 (CH), 28.38 ($3CH_3$). HRMS (ESI) m/z: 377.1465 $[M + Na]^+$, $C_{20}H_{22}N_2O_4Na$ required 377.1472.

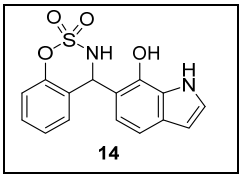
<u>Reaction with 7-hydroxyindole 13. Characterization of compounds 14 and 15.</u>

The aza-Friedel-Crafts reaction using 7-hydroxyindole using as nucleophile was not regioselective and enantioselective. The corresponding products alkylated at C-6 (**14**) and at C-4 (**15**), where obtained in low yields due to the several chromatographic columns made to purify them.



1a + **13** → **14,** 22% rdt., 8% ee + **15**, 24% rdt, 0% ee

2,2 Diòxid de 4-(7-hidroxi-1*H*-indol-4-il)- 3,4-dihidrobenzo[*e*][1,2,3]oxatiazina (14)

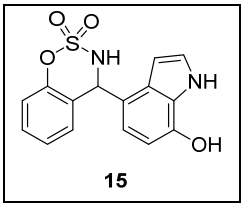


14

Enantiomeric excess (8%) was determined by chiral HPLC (Chiralcel OD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer rt = 27.0 min, minor enantiomer rt = 32.0 min.

Oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.24 (dddd, *J* = 8.2, 7.2, 1.7, 0.8 Hz, 1H), 7.11 (dd, *J* = 3.1, 2.6 Hz, 1H), 7.04 (dd, *J* = 8.3, 1.2 Hz, 1H), 6.99 – 6.90 (m, 2H), 6.84 – 6.80 (m, 1H), 6.51 (d, *J* = 7.7 Hz, 1H), 6.12 – 6.06 (m, 2H), 5.36 (s, 1H), 4.81 (d, *J* = 8.6 Hz, 1H). ^{13}C RMN (75 MHz, $CDCl_3$) δ 151.18 (C), 142.87 (C), 129.41 (CH), 128.51 (CH), 126.28 (C), 125.24 (CH), 125.15 (CH), 122.49 (C), 121.86 (CH), 121.55 (C), 118.64 (CH), 106.14 (CH), 100.61 (CH), 77.20 (C), 61.10 (CH). HRMS (ESI) m/z: 317.0590 $[M + H]^+$, $C_{15}H_{13}N_2O_4S$ required 317.0591.

4-(7-Hydroxy-1*H*-indol-4-yl)-3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (15)

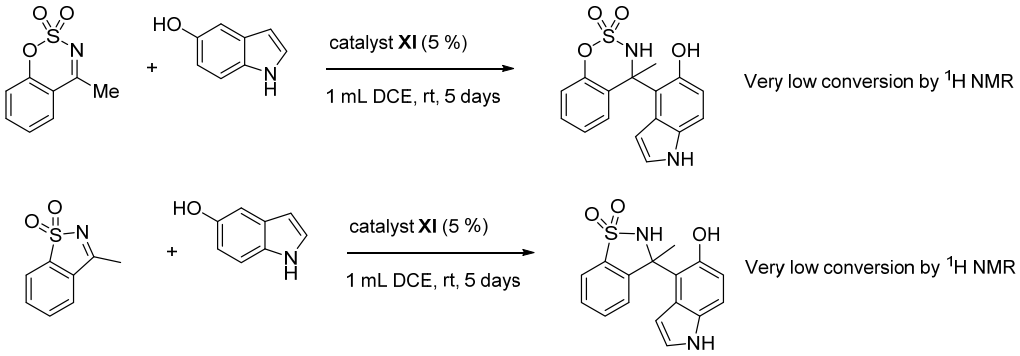


15

Enantiomeric excess (0%) was determined by chiral HPLC (Chiralcel OD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer rt = 12.8 min, minor enantiomer rt = 17.15 min.

Oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.68 (s, 1H), 7.32 – 7.20 (m, 4H), 7.07 – 6.99 (m, 2H), 6.90 (d, *J* = 8.2 Hz, 1H), 6.87 – 6.80 (m, 1H), 6.54 (dd, *J* = 3.1, 2.1 Hz, 1H), 6.10 (s, 1H), 5.75 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.91 (C), 140.12 (C), 131.06 (C), 129.65 (CH), 127.97 (CH), 126.86 (C), 125.66 (CH), 125.45 (CH), 122.48 (C), 121.57 (CH), 118.55 (CH), 115.33 (C), 114.23 (CH), 103.27 (CH), 59.58 (CH). HRMS (ESI) m/z: 317.0592 $[M + H]^+$, $C_{15}H_{13}N_2O_4S$ required 317.0591.

Reaction with cyclic ketimines.



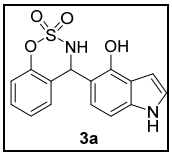
References

[1] L. De Munck, A. Monleón, C. Vila, M. Carmen Muñoz, J. R. Pedro, *Org. Biomol. Chem.*, **2015**, *13*, 7393.

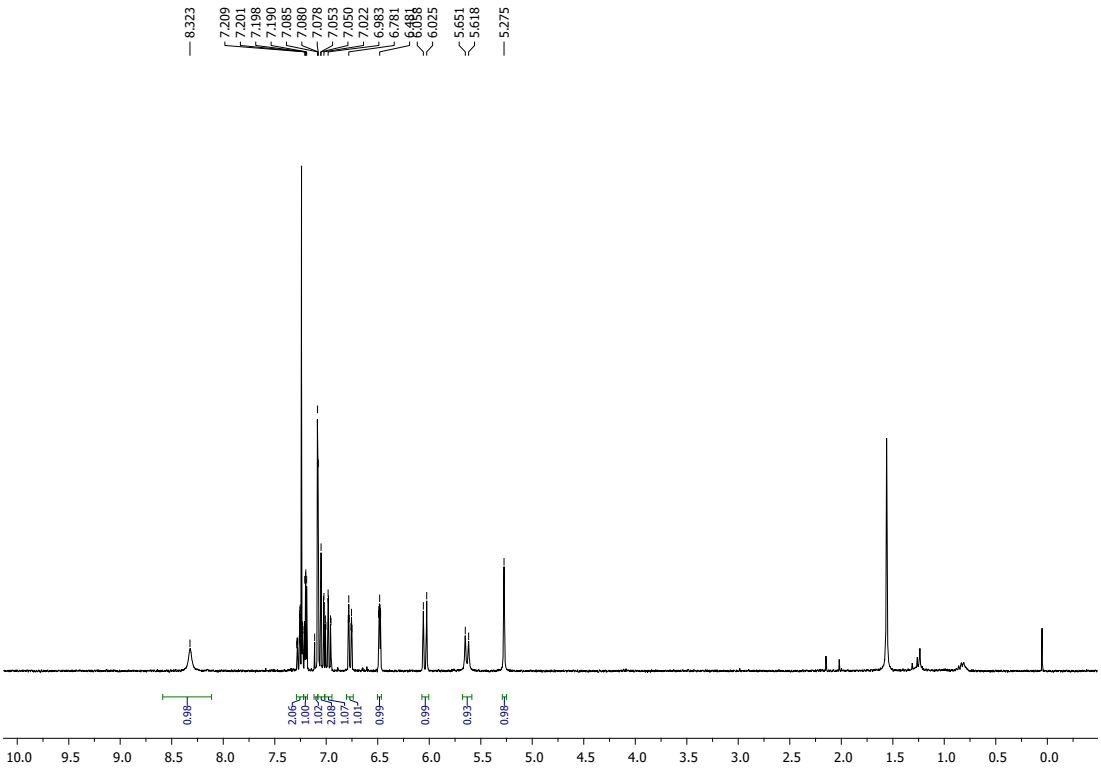
[2] H. Li, Y. Wang, L Tang, L. Deng, *J. Am. Chem. Soc.*, **2004**, *126*, 9906.

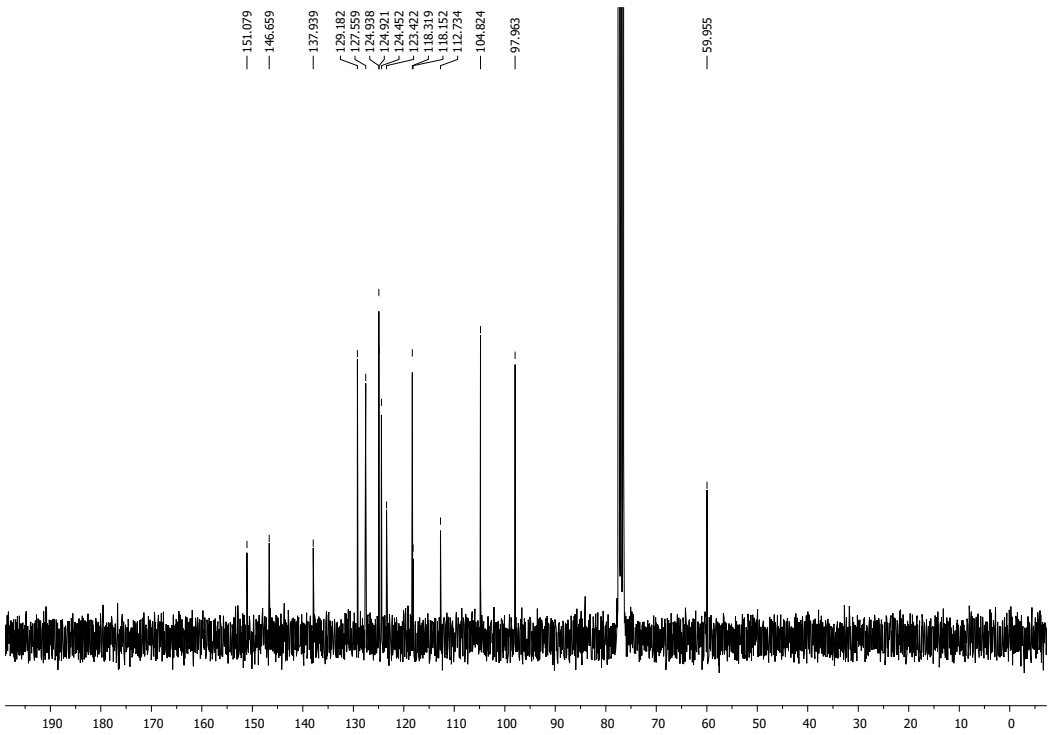
^{1}H and ^{13}C NMR spectra and HPLC traces

4-(4-Hydroxy-1*H*-indol-5-yl)-3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (3a)

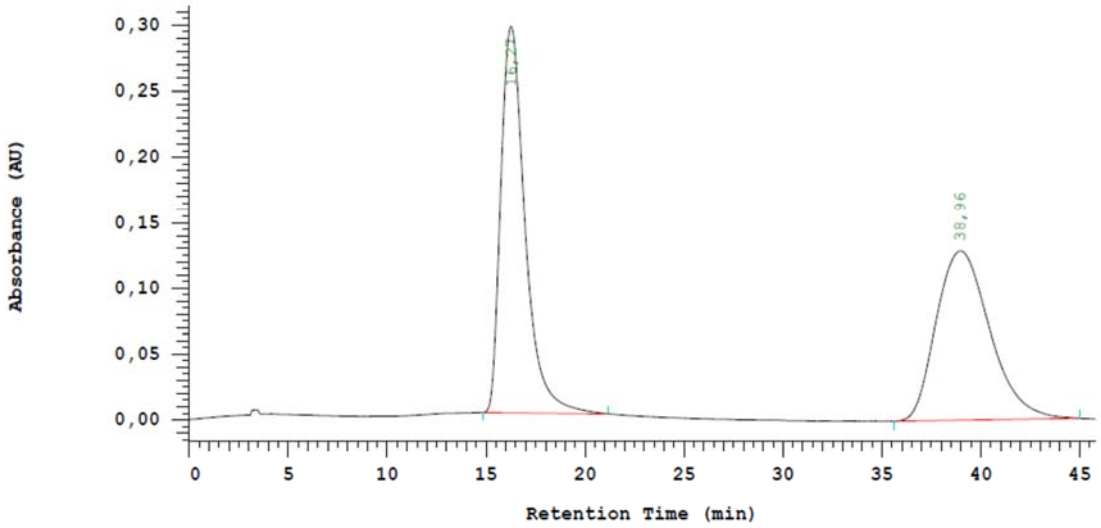


3a



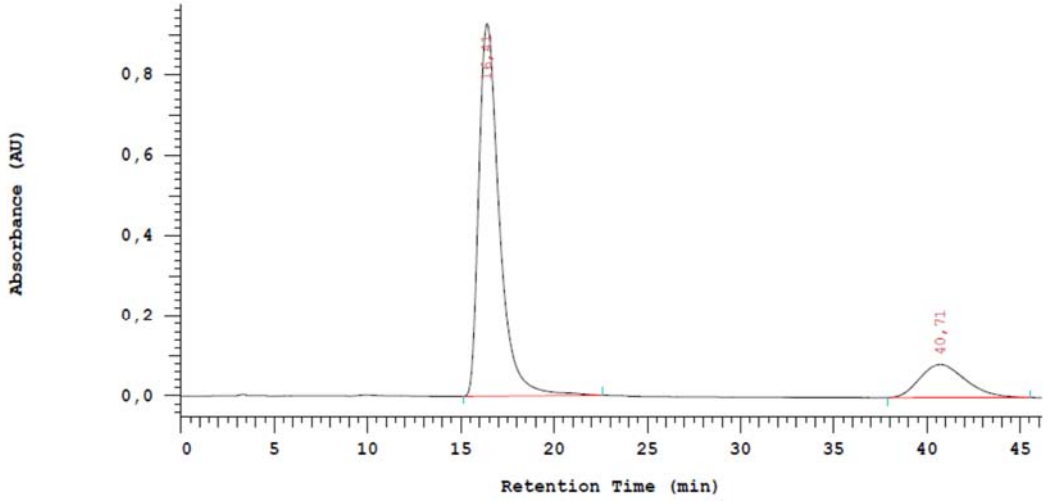


Sample Name: AT-20A ODH 8020 1 mL Vial Number: 1



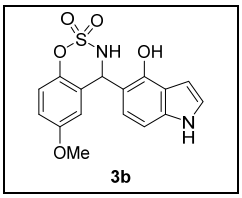
No.	RT	Area	Area %	Name
1	16,27	12440640	50,760	
2	38,96	12067940	49,240	

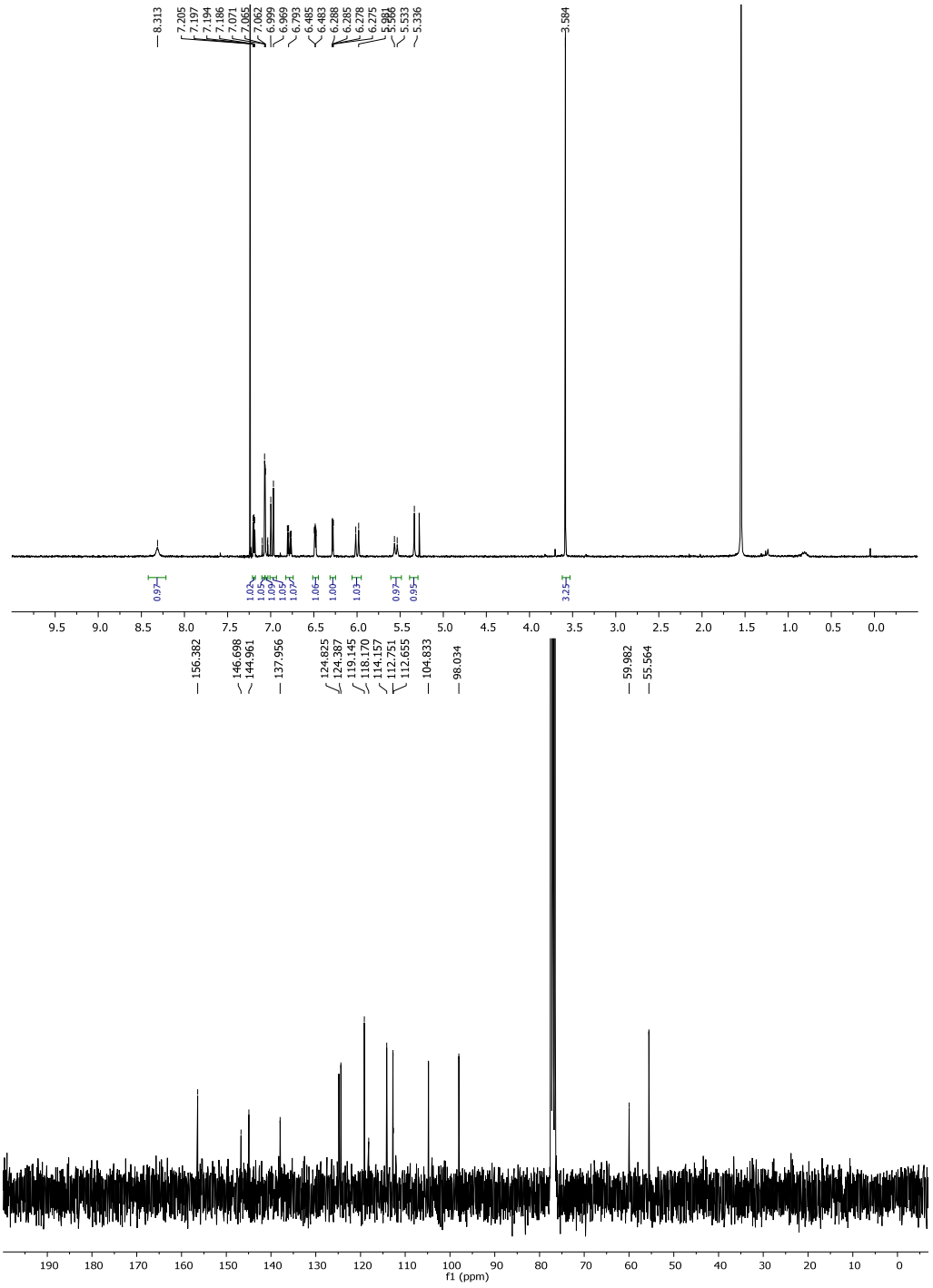
Sample Name: AT-70A ODH 8020 1 mL Vial Number: 1



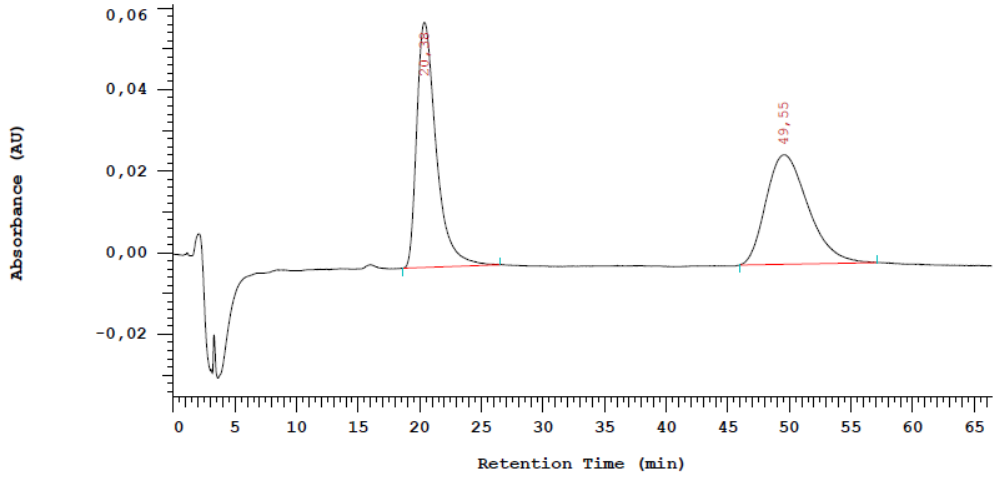
No.	RT	Area	Area %	Name
1	16,41	35251718	83,423	
2	40,71	7004710	16,577	

4-(4-Hydroxy-1*H*-indol-5-yl)-6-methoxy-3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (3b)



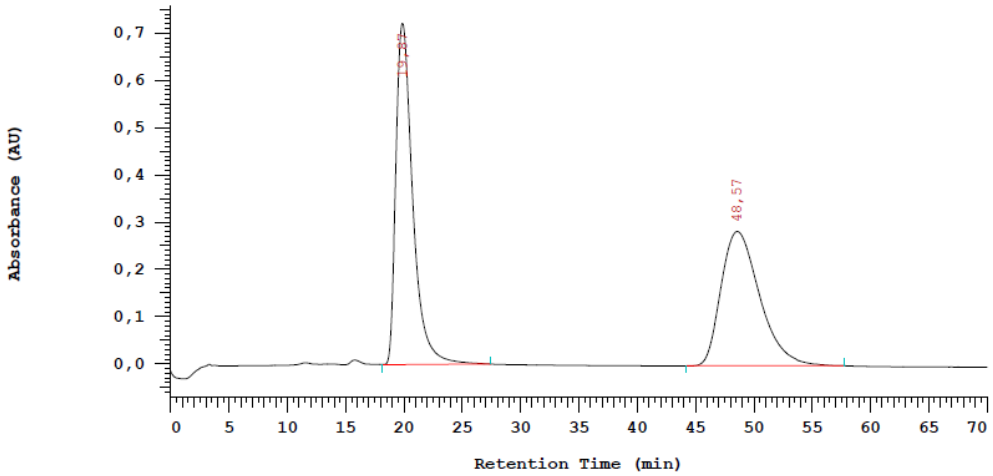


Sample Name: AT-92A ODH 8020 1 mL Vial Number: 1



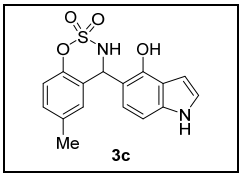
No.	RT	Area	Area %	Name
1	20,38	3278580	50,875	
2	49,55	3165760	49,125	
		6444340	100,000	

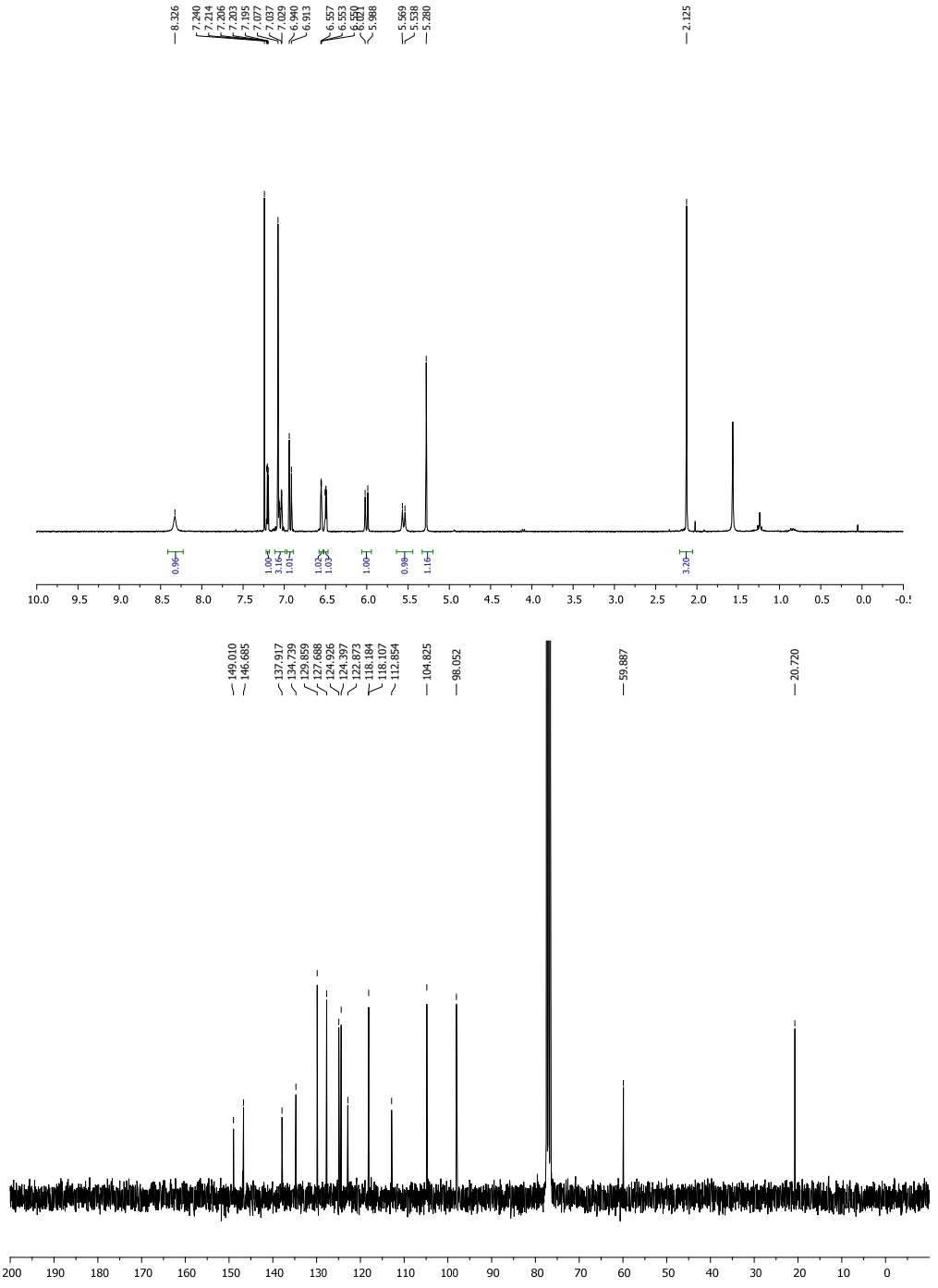
Sample Name: AT-93A ODH 8020 1 mL Vial Number: 1



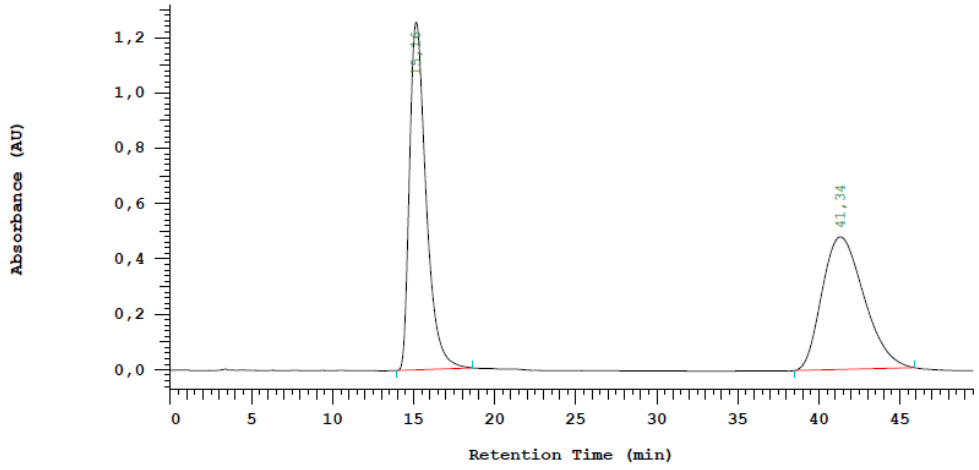
No.	RT	Area	Area %	Name
1	19,87	35945884	52,349	
2	48,57	32719731	47,651	
		68665615	100,000	

4-(4-Hydroxy-1*H*-indol-5-yl)-6-methyl-3,4-dihydrobenzo[$_e$][1,2,3]oxathiazine 2,2-dioxide (3c)



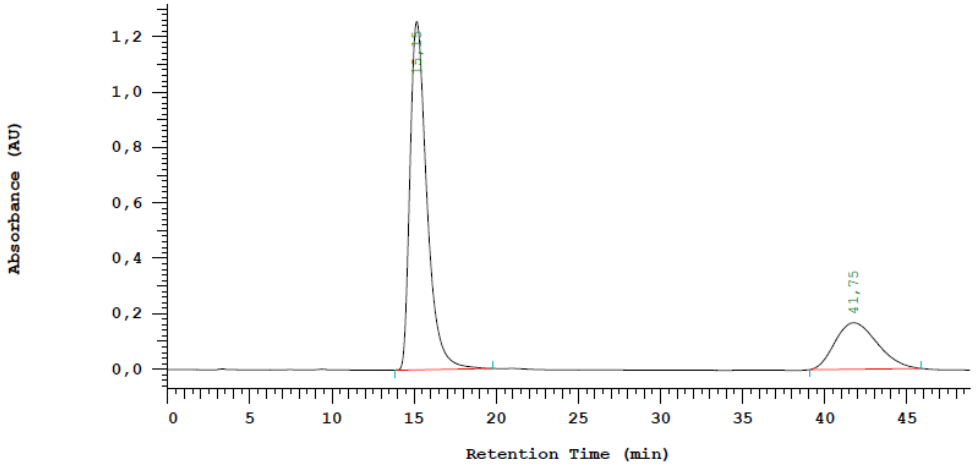


Sample Name: AT-88A ODH 8020 1 mL Vial Number: 1



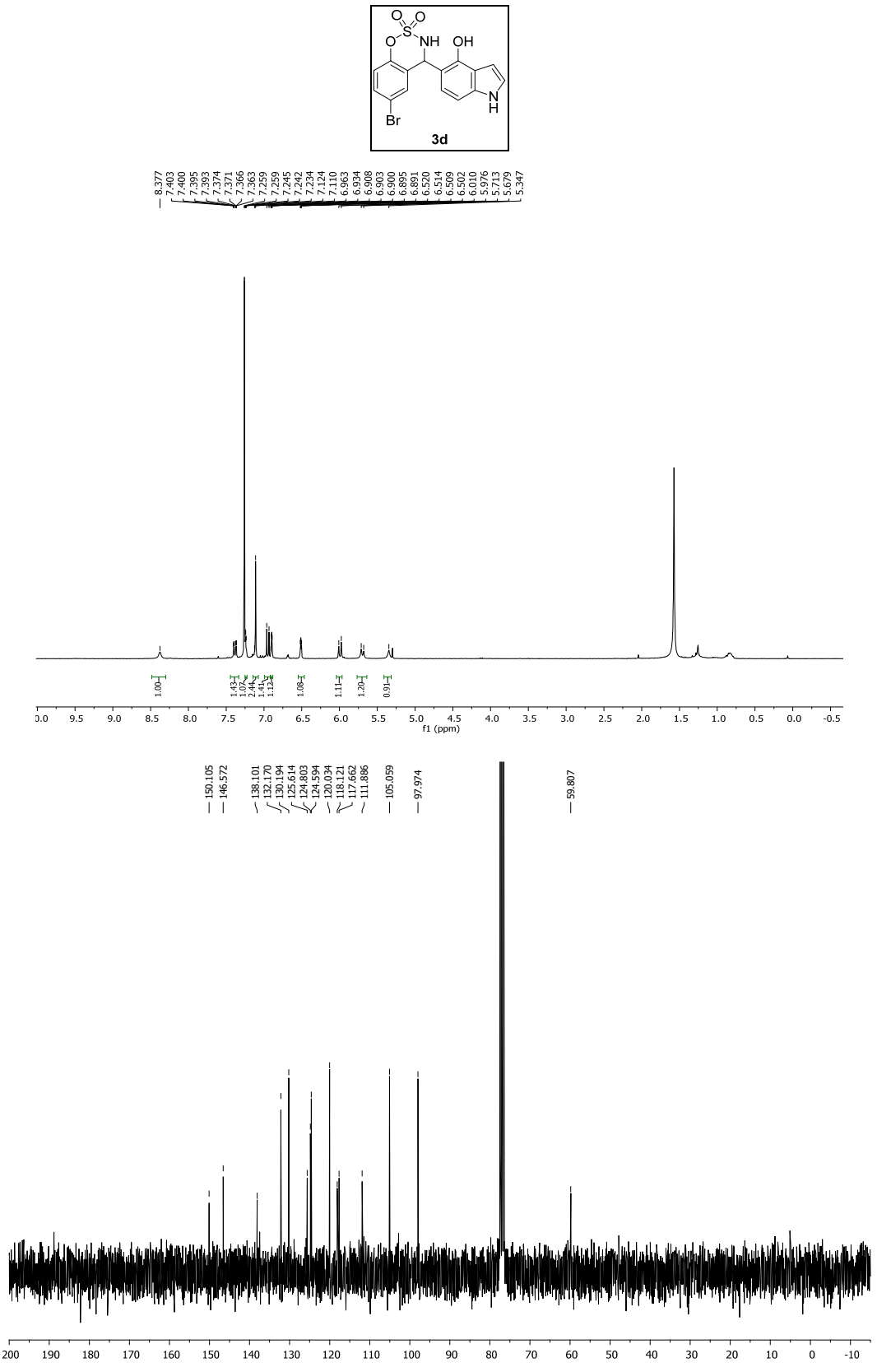
No.	RT	Area	Area %	Name
1	15,16	44256595	50,757	
2	41,34	42936979	49,243	
		87193574	100,000	

Sample Name: AT-90A ODH 8020 1 mL Vial Number: 1

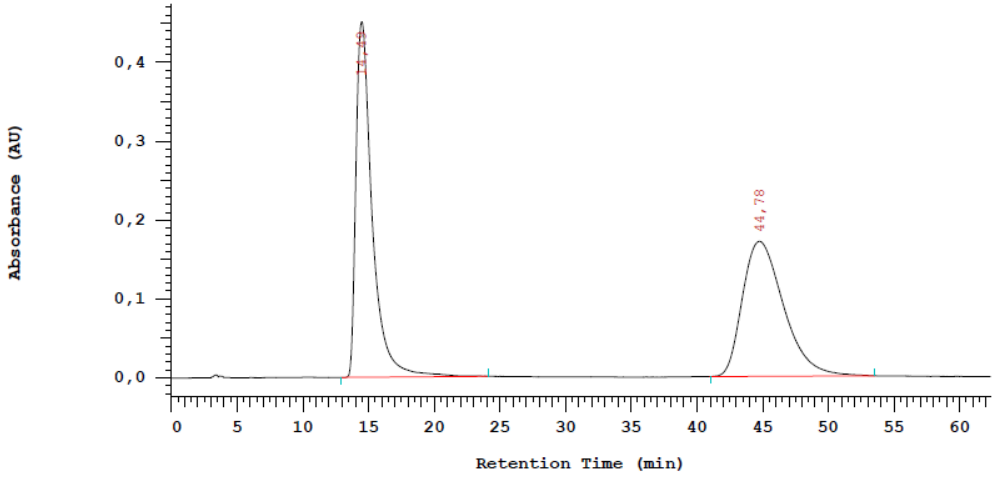


No.	RT	Area	Area %	Name
1	15,15	44540140	74,898	
2	41,75	14927265	25,102	
		59467405	100,000	

6-Bromo-4-(4-hydroxy-1*H*-indol-5-yl)-3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (3d)

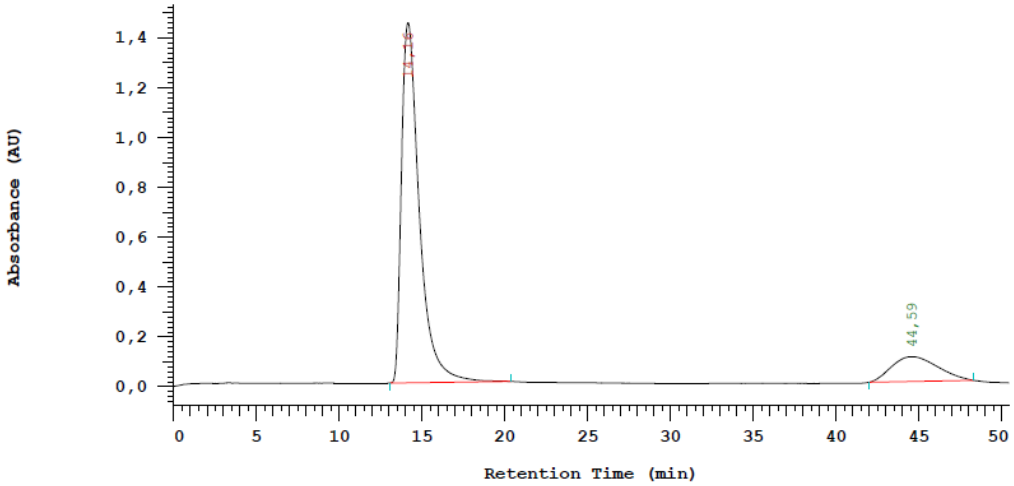


Sample Name: AT-102A ODH 8020 1mL Vial Number: 1



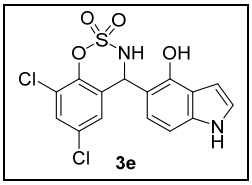
No.	RT	Area	Area %	Name
1	14,49	19268000	50,947	
2	44,78	18552030	49,053	
		37820030	100,000	

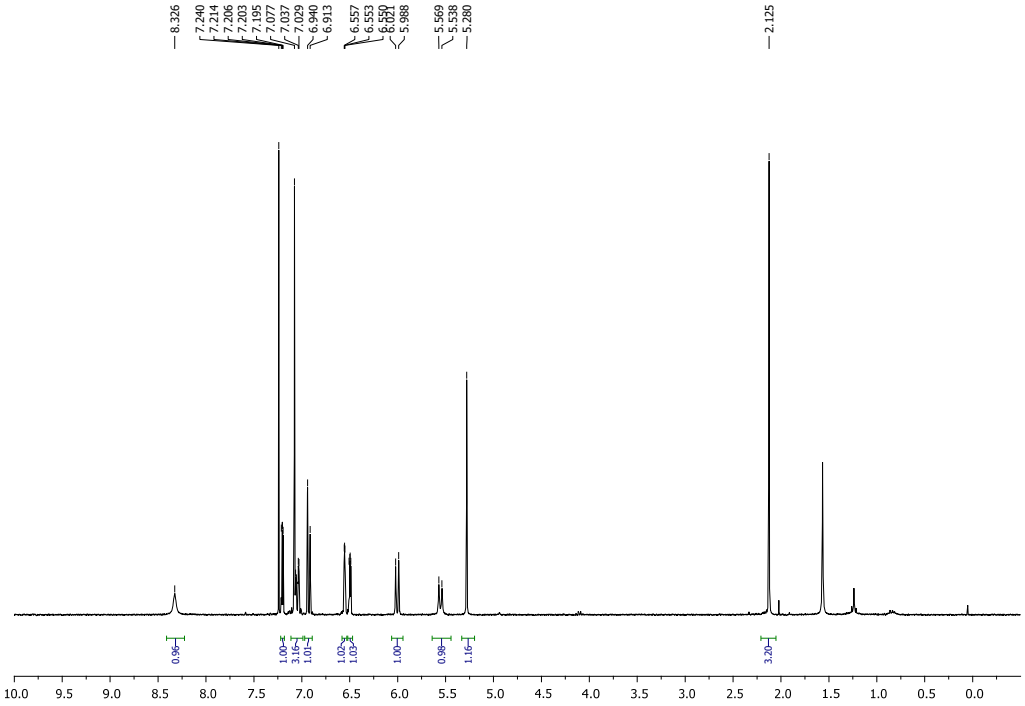
Sample Name: AT-103A ODH 8020 1 mL Vial Number: 1

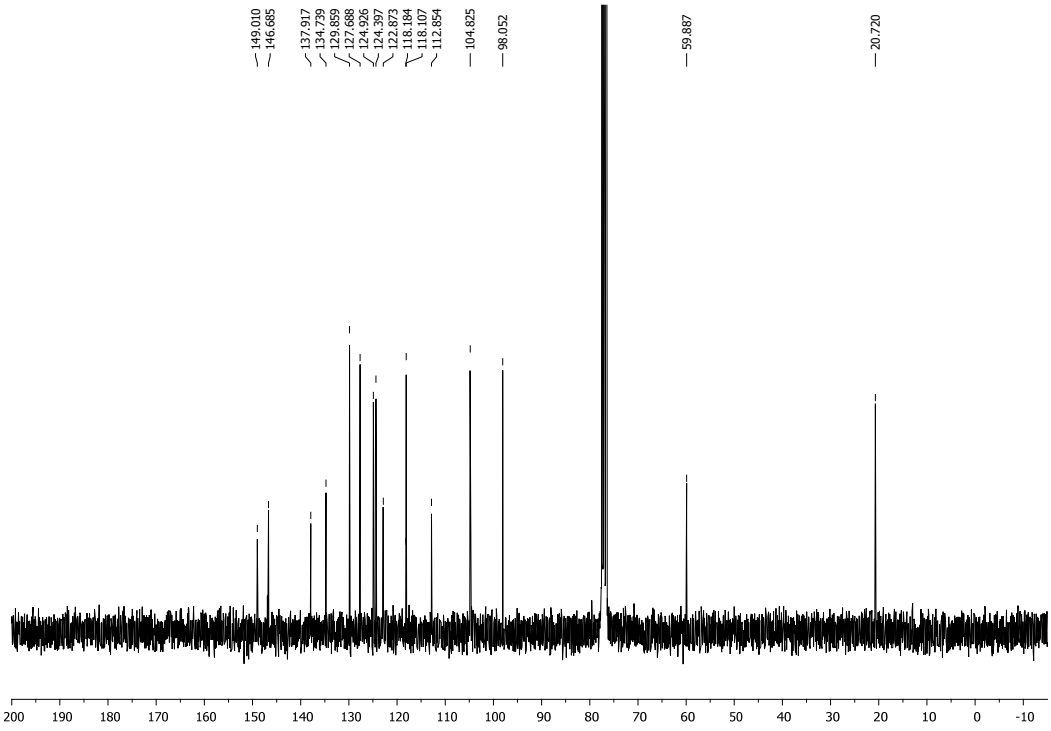


No.	RT	Area	Area %	Name
1	14,16	53869363	84,937	
2	44,59	9553300	15,063	
		63422663	100,000	

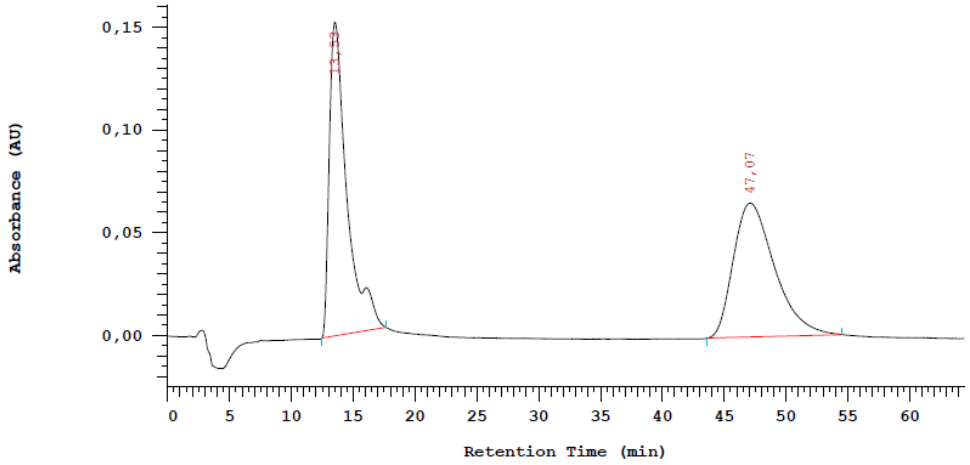
6,8-Dichloro-4-(4-hydroxy-1*H*-indol-5-yl)-3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (3e)





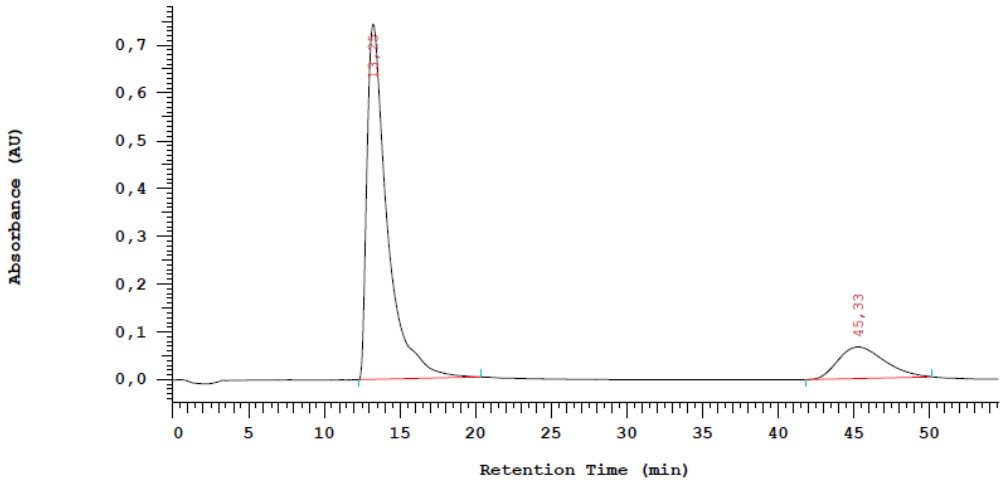


Sample Name: AT-89A ODH 8020 1 mL Vial Number: 1



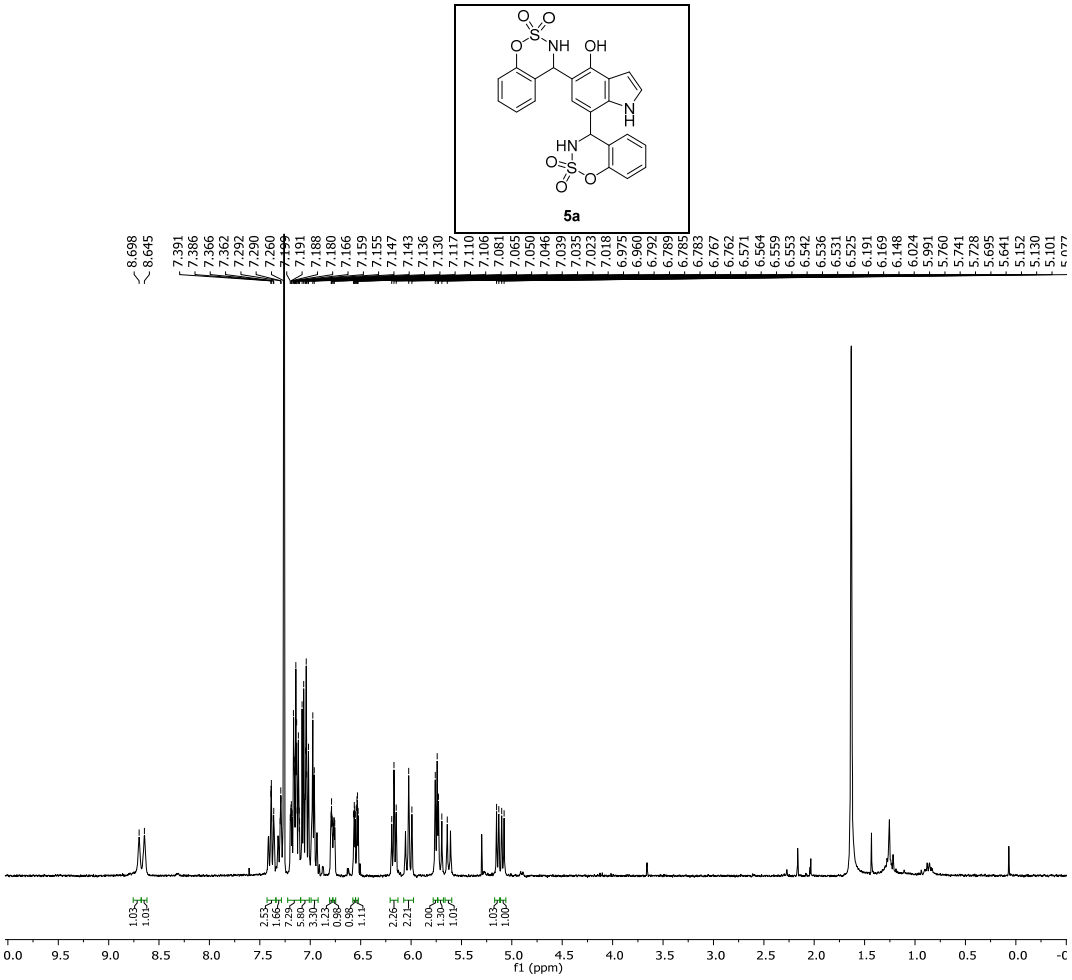
No.	RT	Area	Area %	Name
1	13,53	7510390	49,887	
2	47,07	7544564	50,113	
		15054954	100,000	

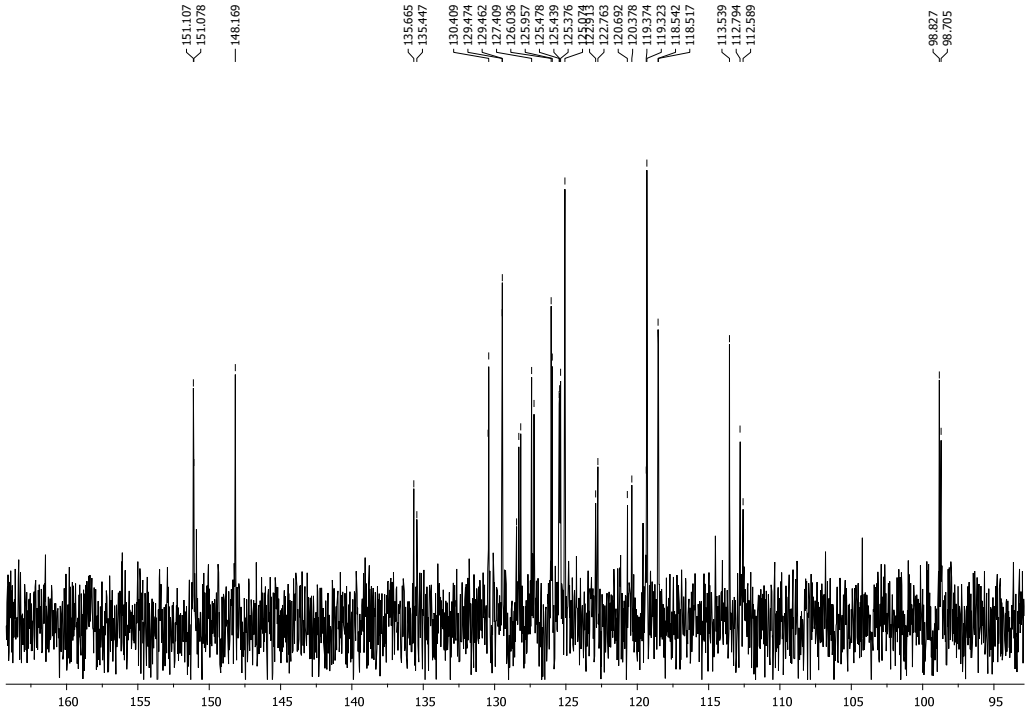
Sample Name: AT-91A ODH 8020 1 mL Vial Number: 1



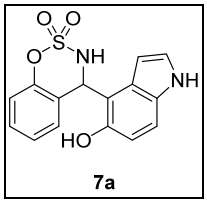
No.	RT	Area	Area %	Name
1	13,25	34326828	83,091	
2	45,33	6985710	16,909	
		41312538	100,000	

4,4'-(4-Hydroxy-1*H*-indole-5,7-diyl)bis(3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide) (5a)

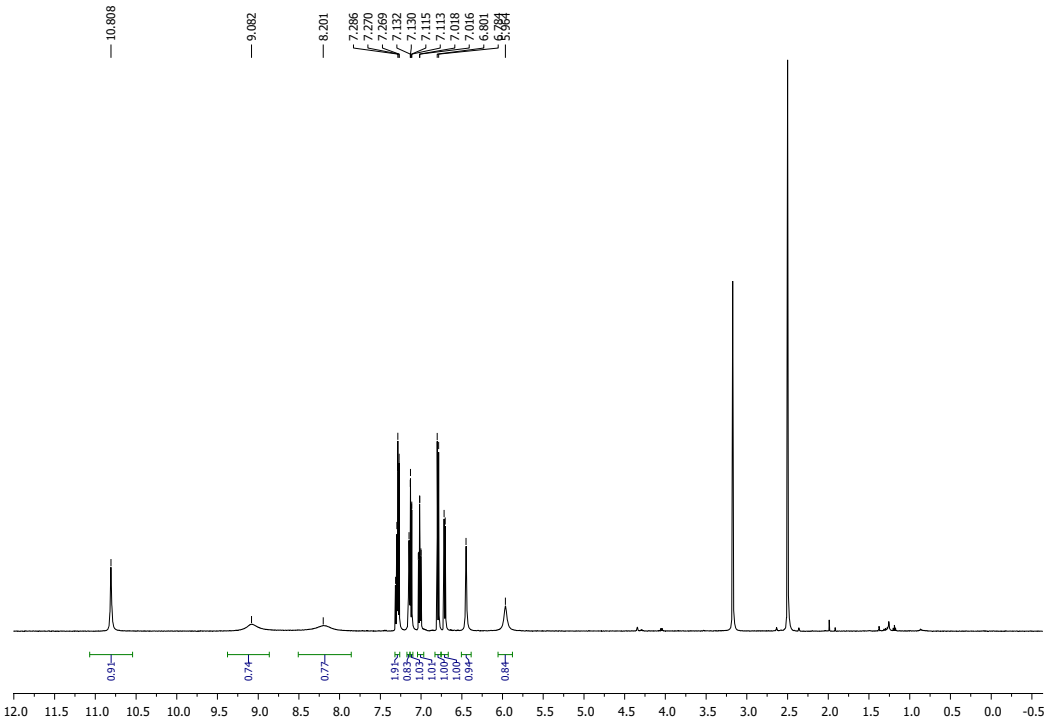


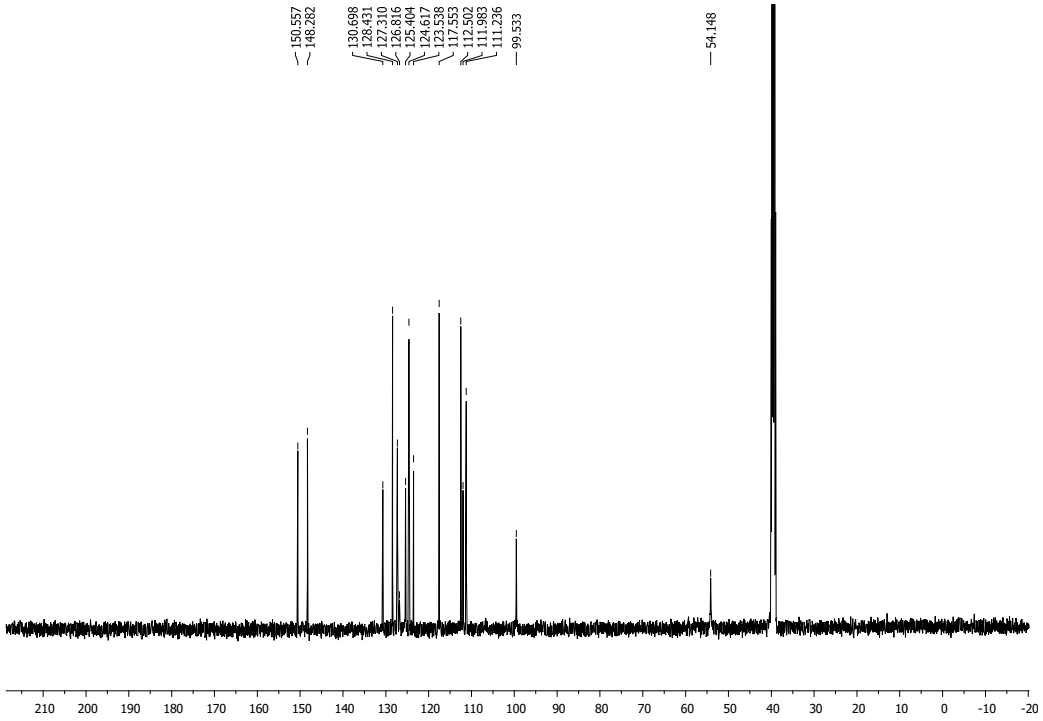


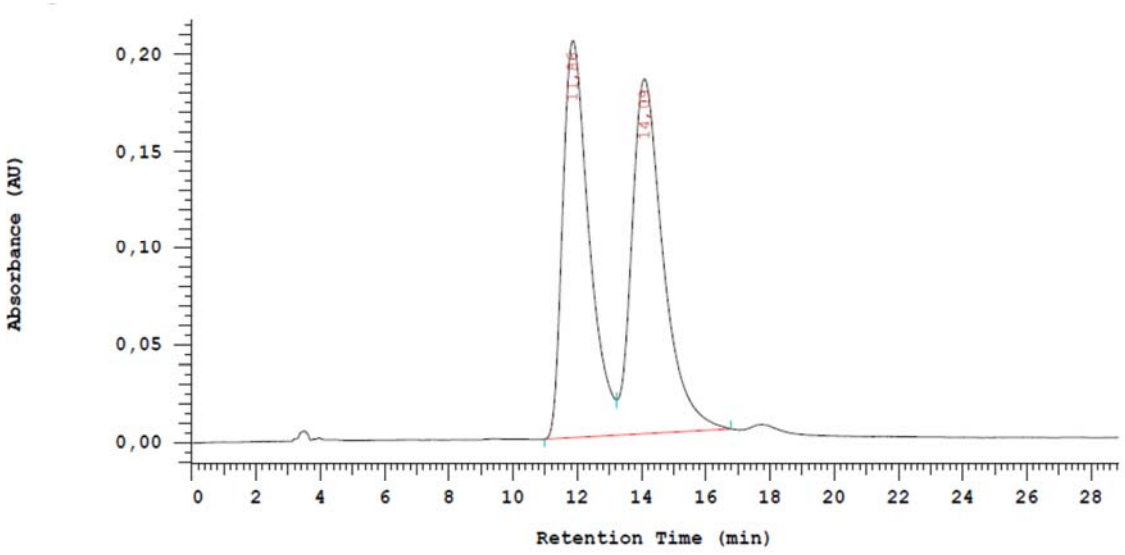
4-(5-Hydroxy-1*H*-indol-4-yl)-3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (7a)



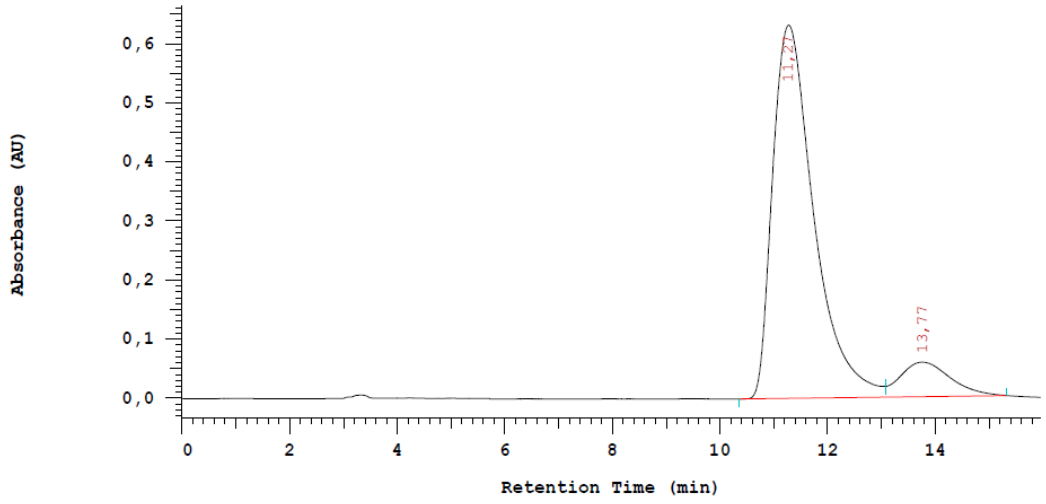
7a





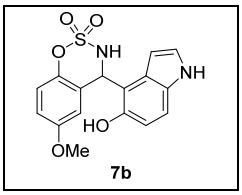


No.	RT	Area	Area %	Name
1	11,86	5814261	48,261	
2	14,09	6233228	51,739	

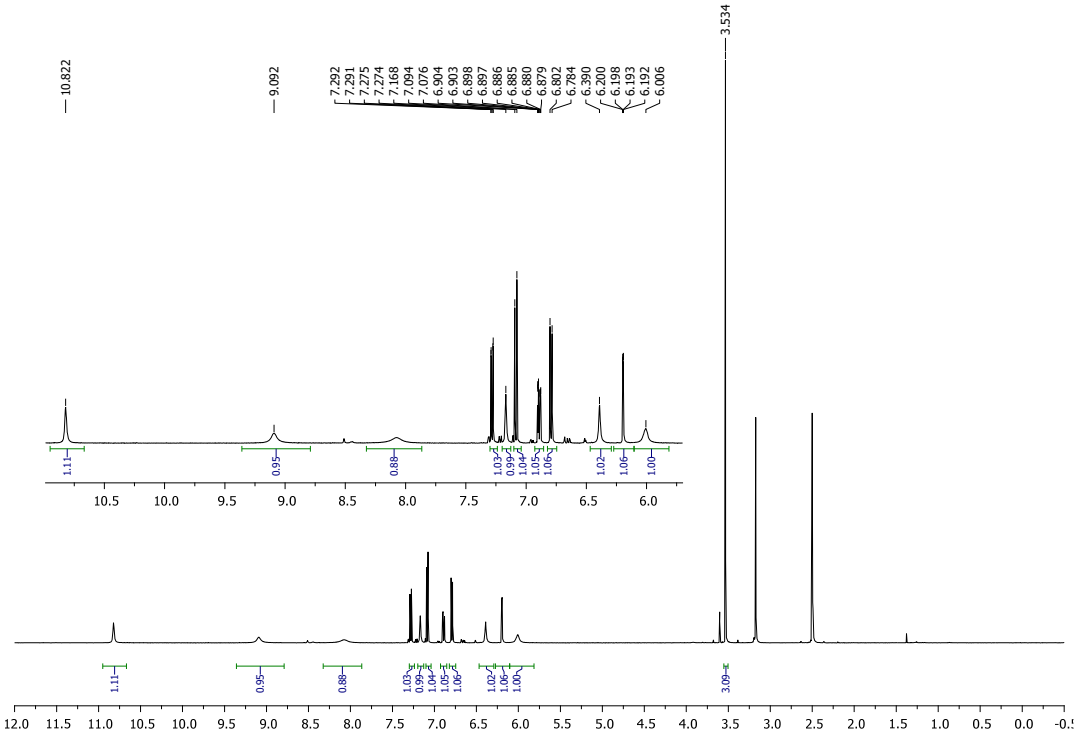


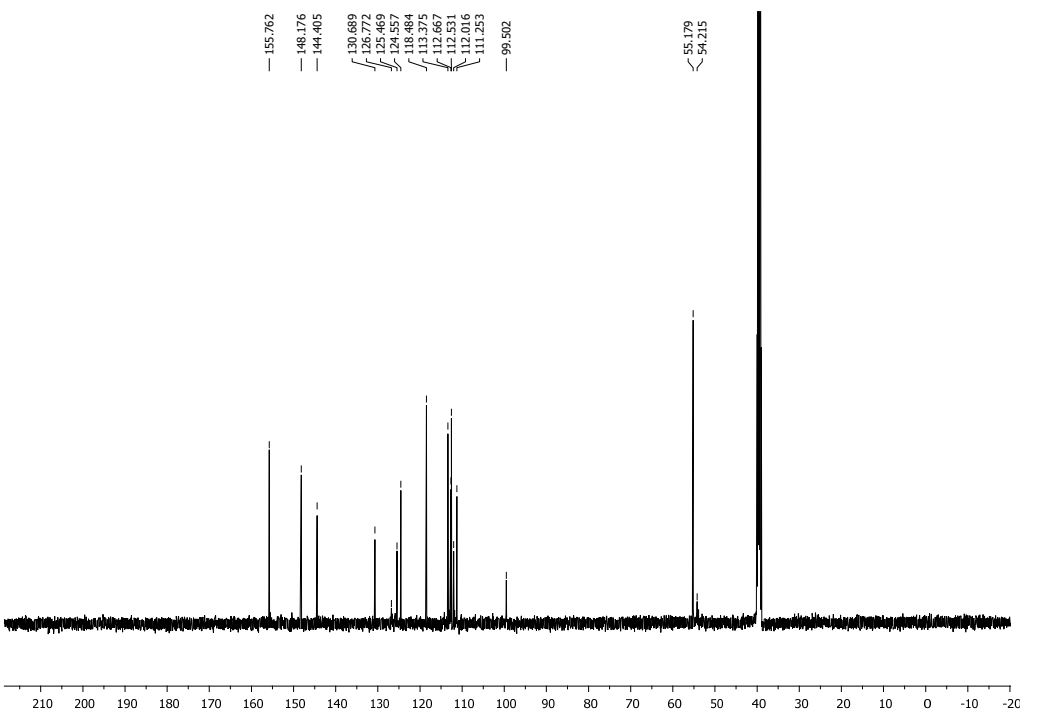
No.	RT	Area	Area %	Name
1	11,27	16794472	89,934	
2	13,77	1879687	10,066	

4-(5-Hydroxy-1*H*-indol-4-yl)-6-methoxy-3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (7b)

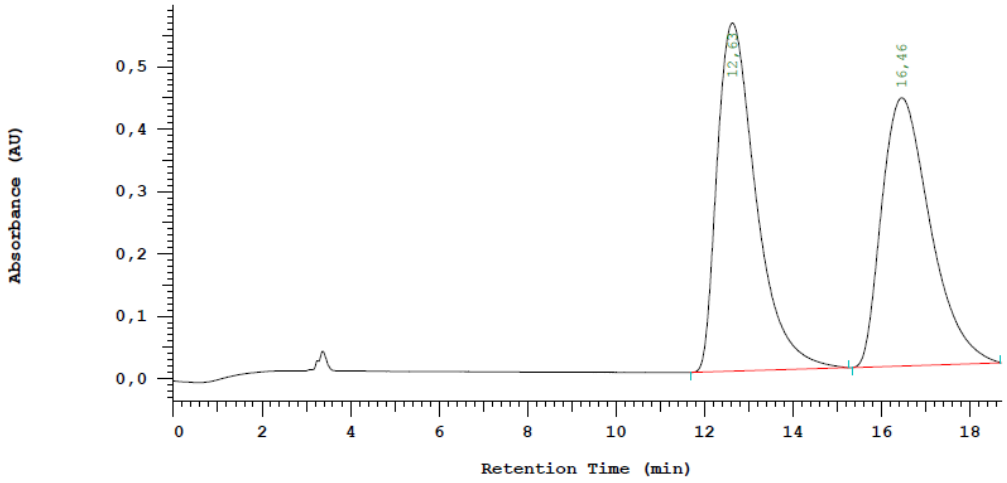


7b



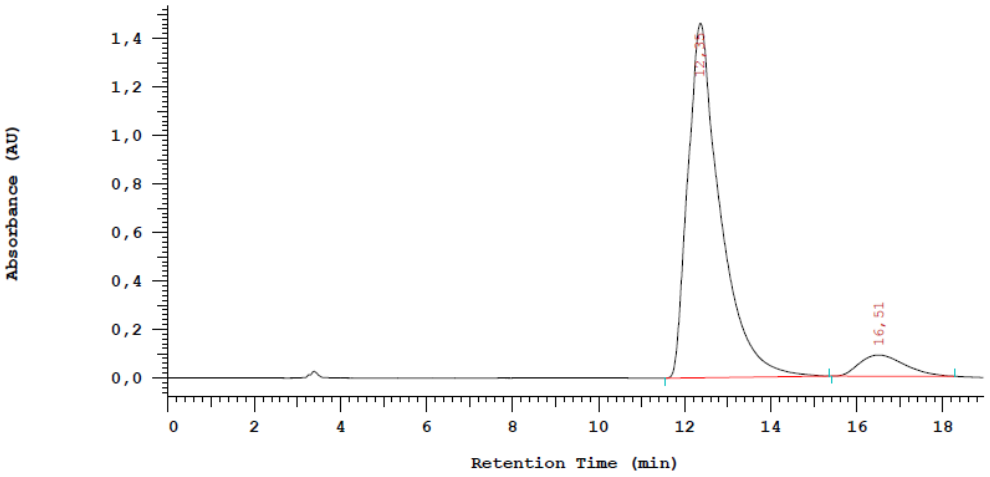


Sample Name: AT-86 ODH 8020 1 mL Vial Number: 1



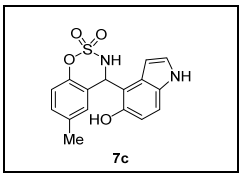
No.	RT	Area	Area %	Name
1	12,63	17121915	51,145	
2	16,46	16355310	48,855	
		33477225	100,000	

Sample Name: AT-84 ODH 8020 1 mL Vial Number: 1

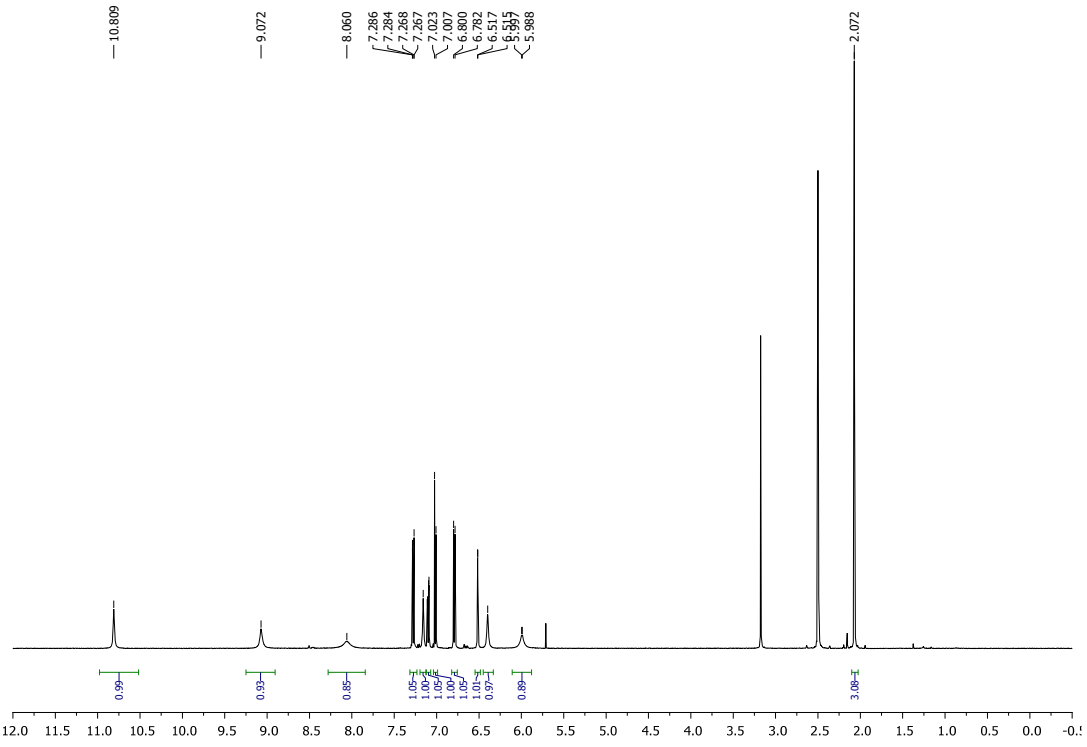


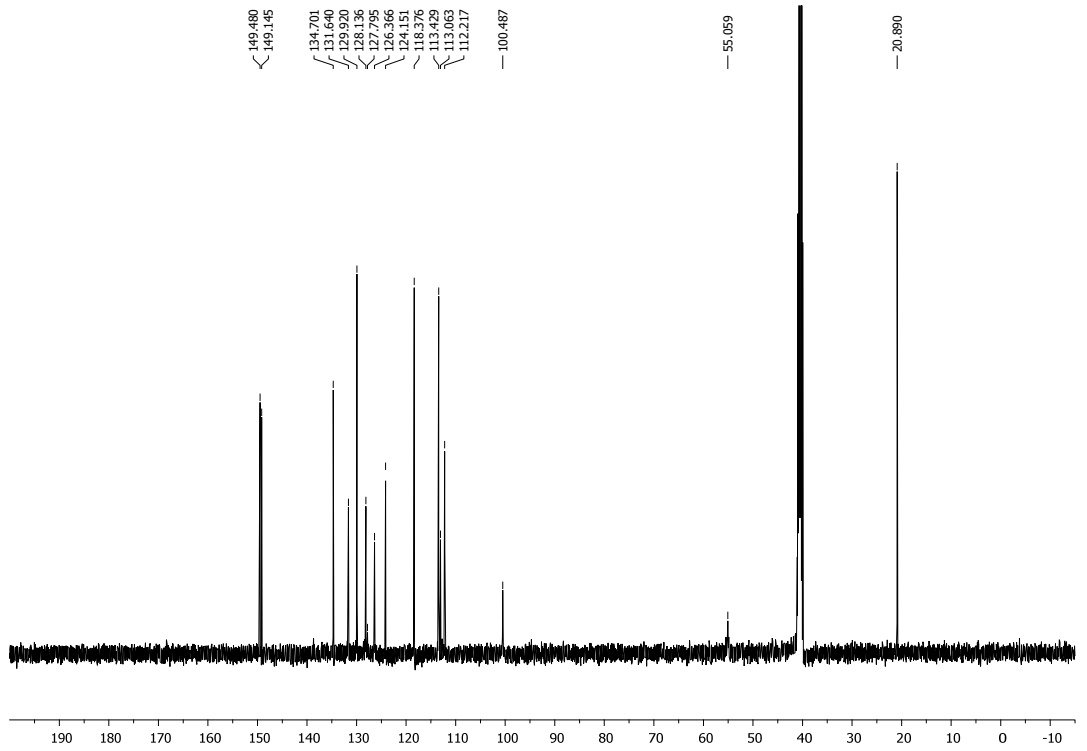
No.	RT	Area	Area %	Name
1	12,35	38230153	92,312	
2	16,51	3183775	7,688	
		41413928	100,000	

4-(5-Hydroxy-1*H*-indol-4-yl)-6-methyl-3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (7c)

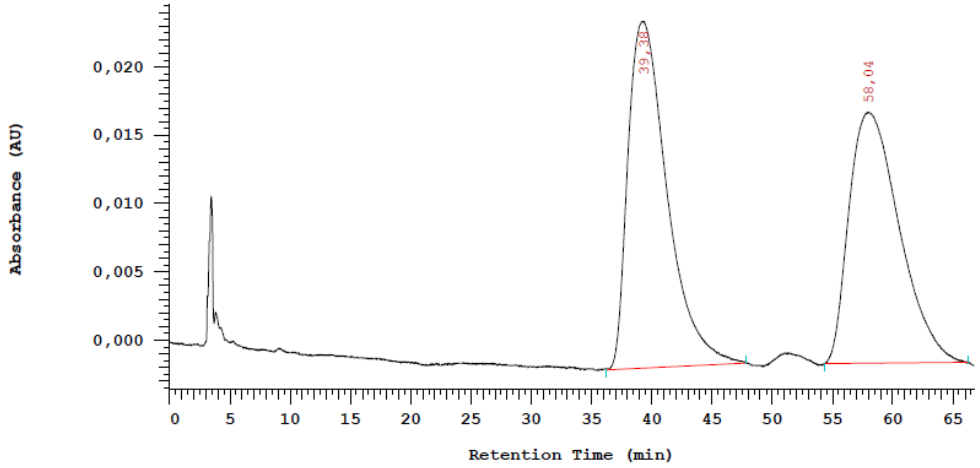


7c



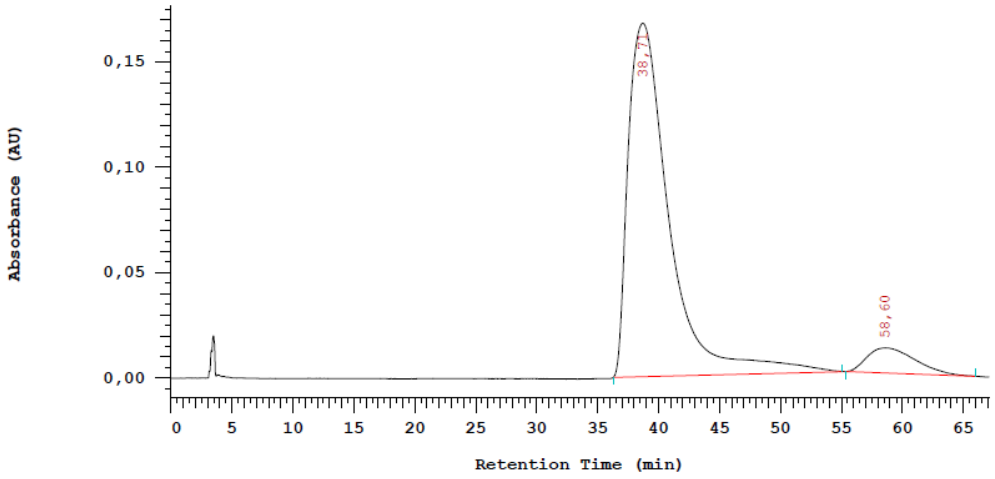


Sample Name: AT-94 ODH 9010 1 mL Vial Number: 1



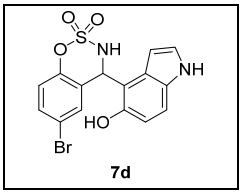
No.	RT	Area	Area %	Name
1	39,38	2853850	51,828	
2	58,04	2652570	48,172	
		5506420	100,000	

Sample Name: AT-96 ODH 9010 1 mL Vial Number: 1

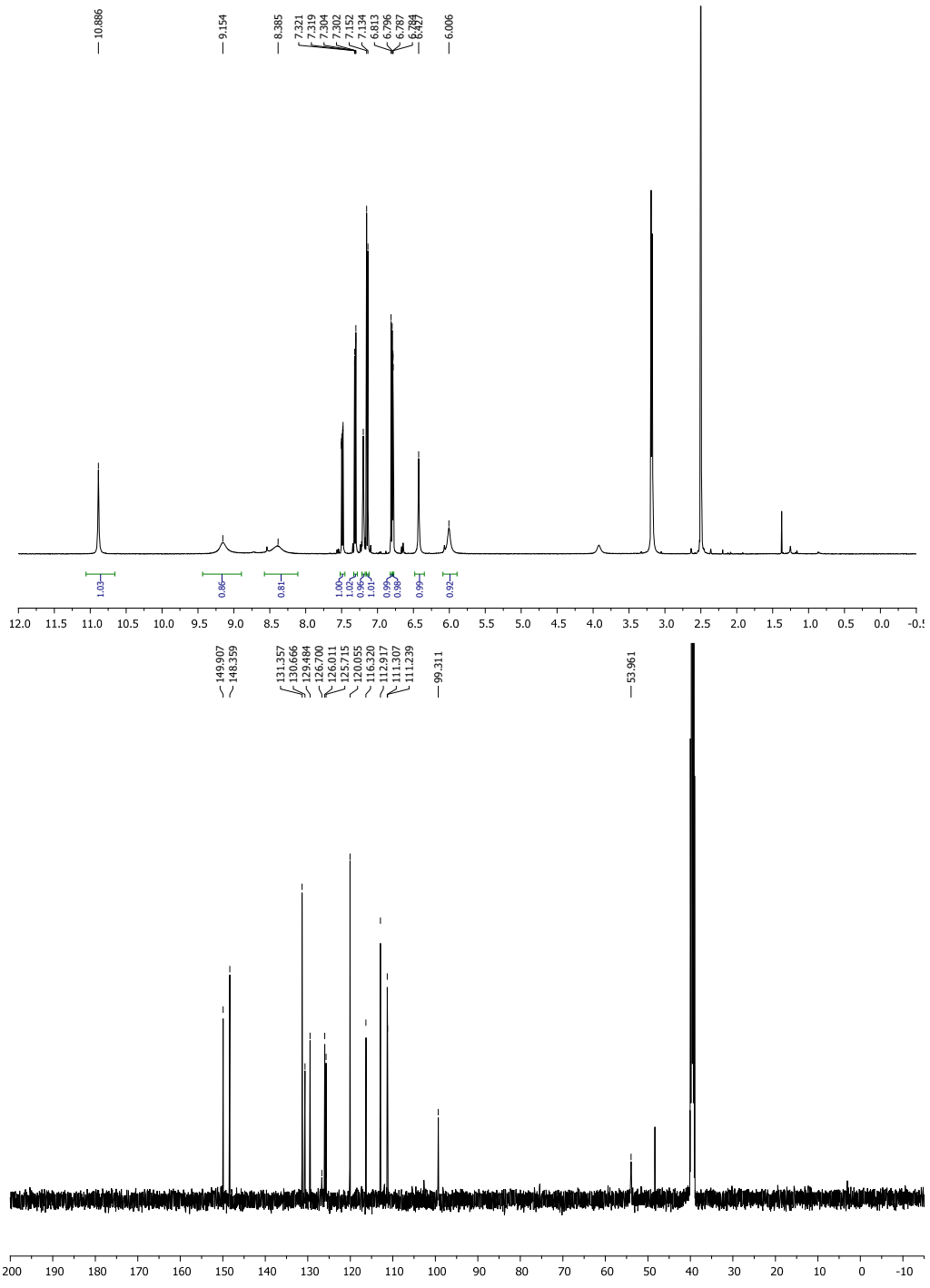


No.	RT	Area	Area %	Name
1	38,71	19604720	92,289	
2	58,60	1638110	7,711	
		21242830	100,000	

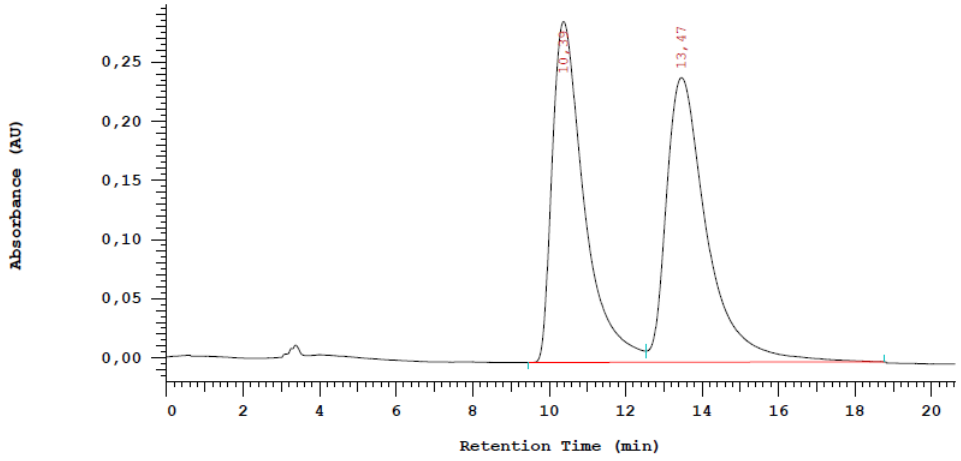
6-Bromo-4-(5-hydroxy-1*H*-indol-4-yl)-3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (7d)



7d

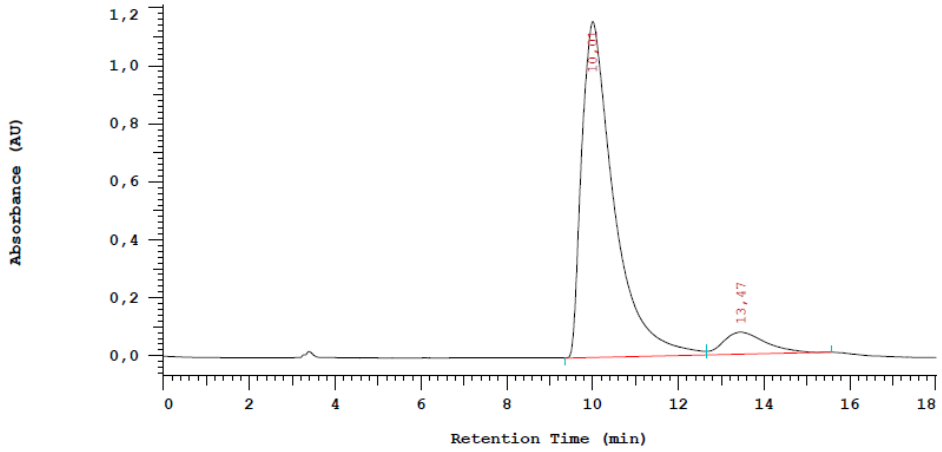


Sample Name: AT-87 ODH 8020 1 mL Vial Number: 1



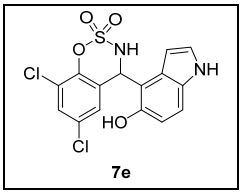
No.	RT	Area	Area %	Name
1	10,39	8390546	48,630	
2	13,47	8863183	51,370	
		17253729	100,000	

Sample Name: AT-85 ODH 8020 1 mL Vial Number: 1

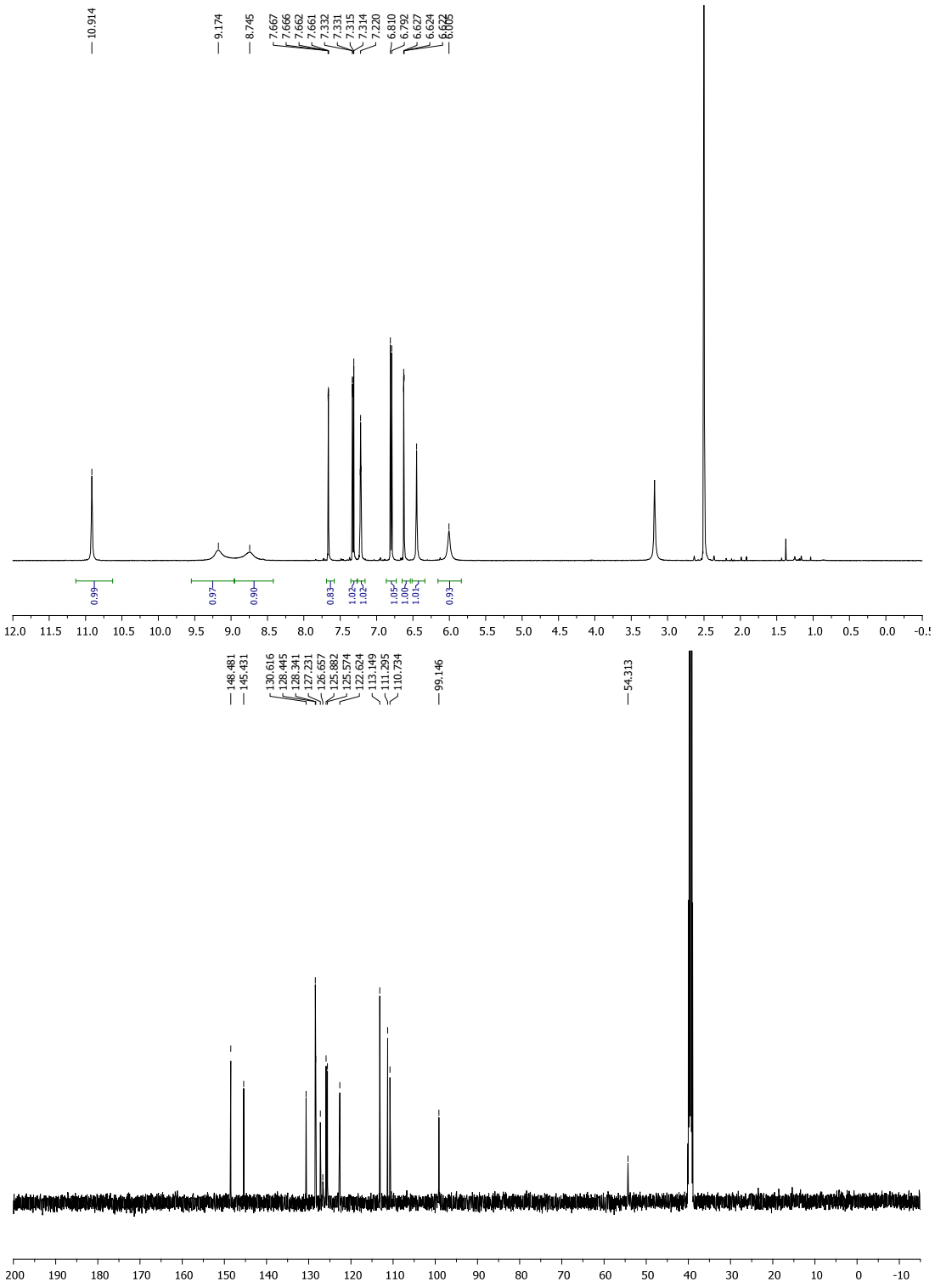


No.	RT	Area	Area %	Name
1	10,01	30216950	92,087	
2	13,47	2596544	7,913	
		32813494	100,000	

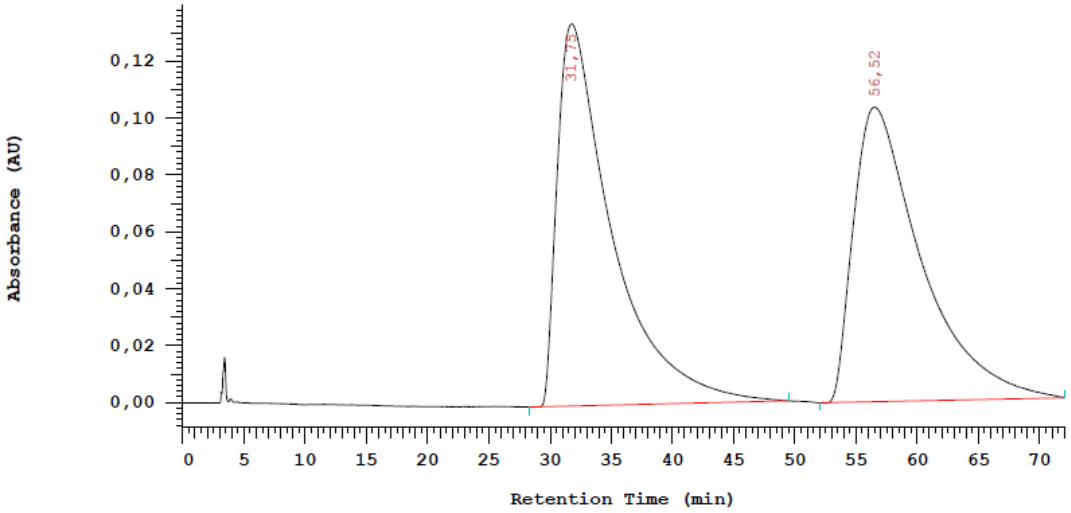
6,8-Dichloro-4-(5-hydroxy-1*H*-indol-4-yl)-3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (7e)



7e

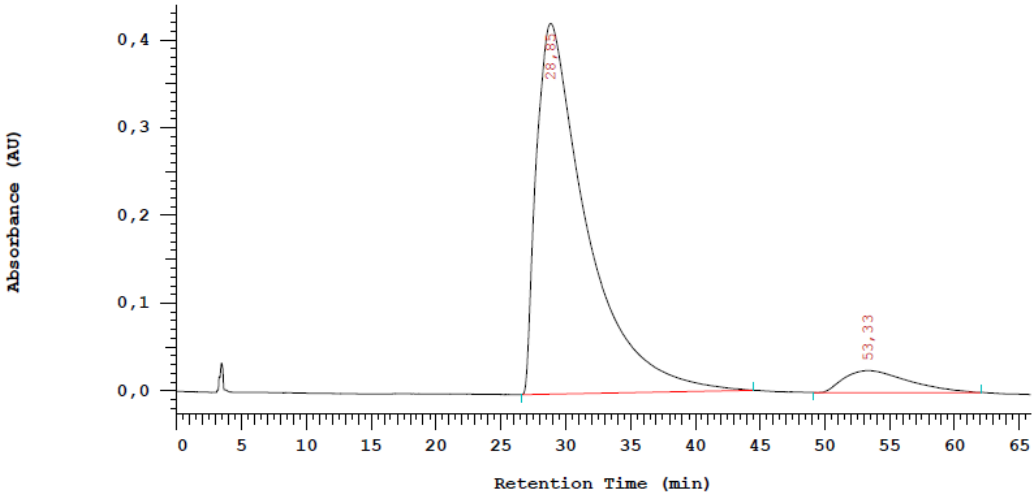


Sample Name: AT-95 ODH 9010 1 mL Vial Number: 1



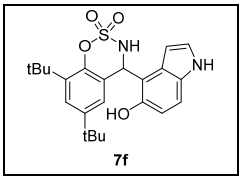
No.	RT	Area	Area %	Name
1	31,75	20751880	51,139	
2	56,52	19827395	48,861	
		40579275	100,000	

Sample Name: AT-97 ODH 8020 1 mL Vial Number: 1

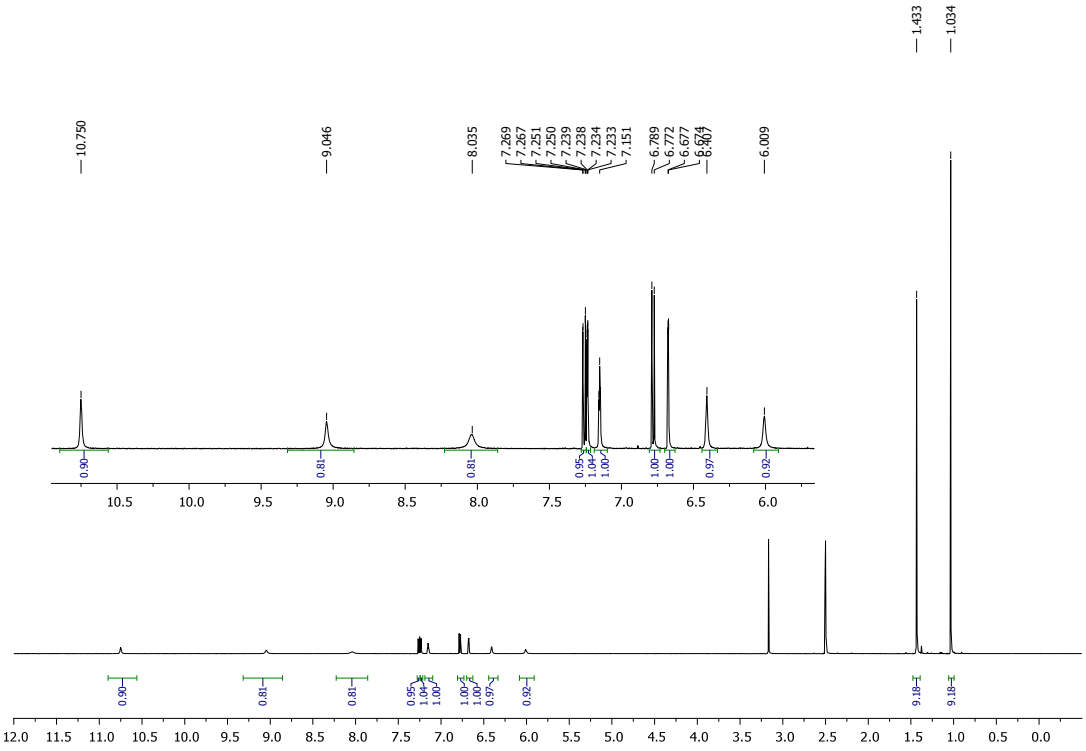


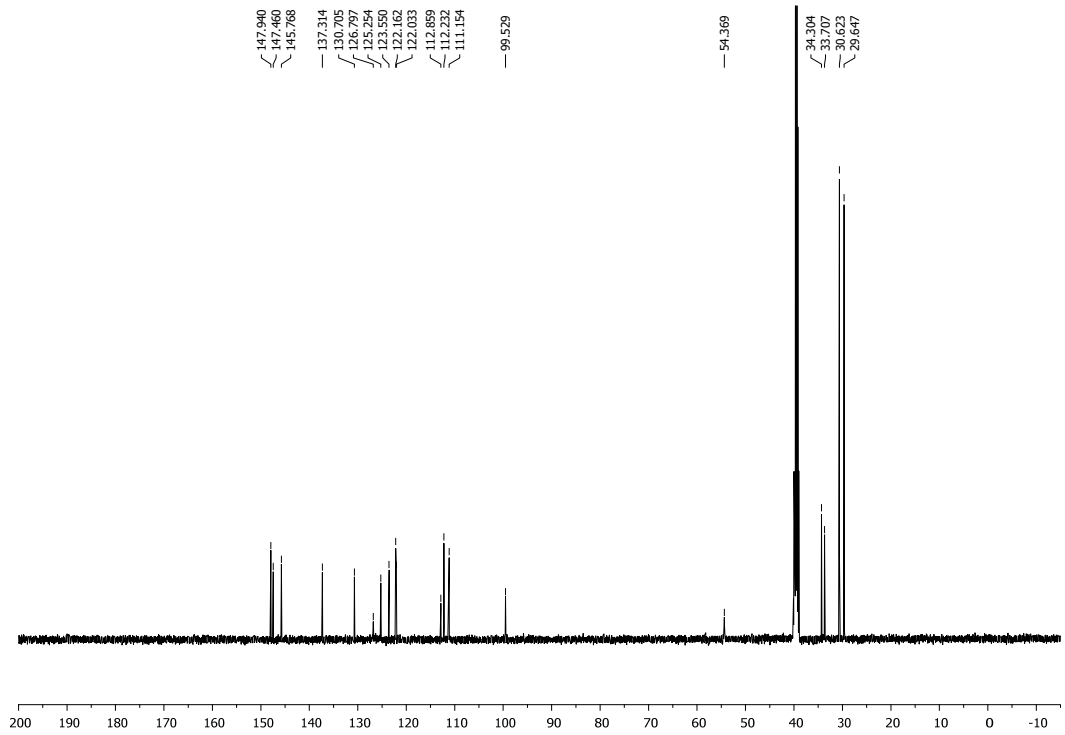
No.	RT	Area	Area %	Name
1	28,85	56817017	92,875	enanti (-)
2	53,33	4358720	7,125	
		61175737	100,000	

6,8-Di-*tert*-butyl-4-(5-hydroxy-1*H*-indol-4-yl)-3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (7f)

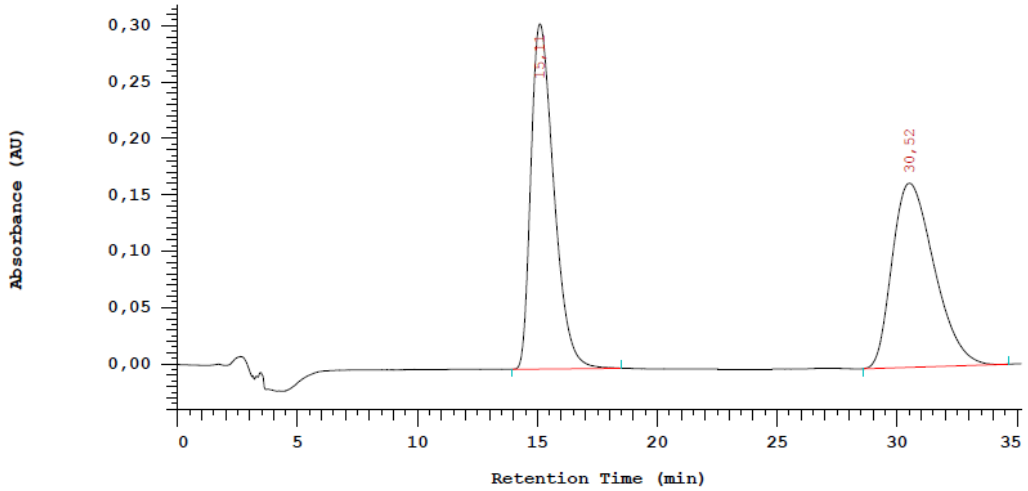


7f



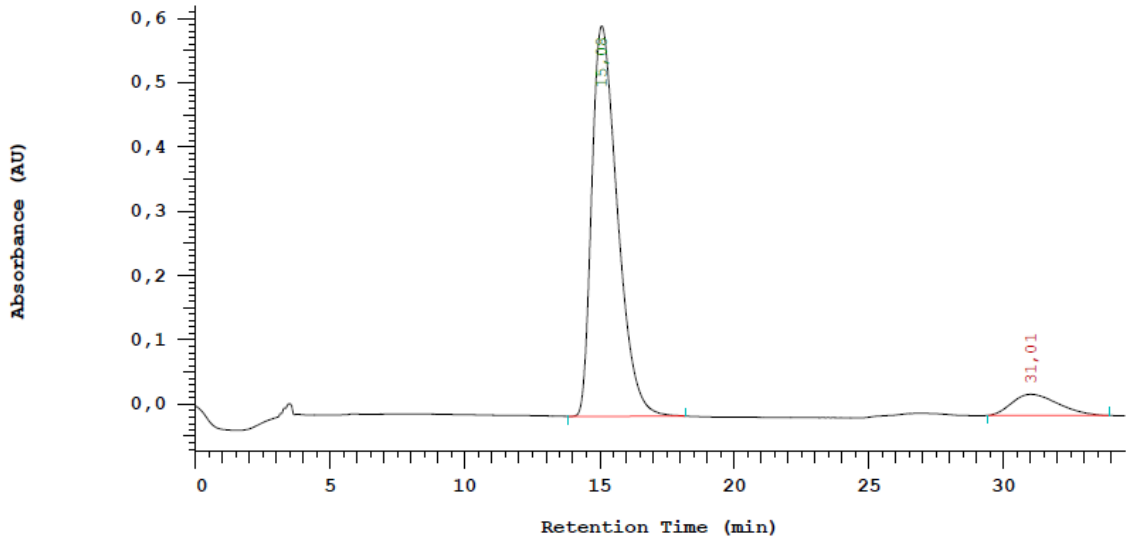


Sample Name: AT-99 ODH 9010 1mL Vial Number: 1



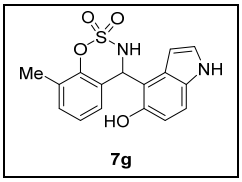
No.	RT	Area	Area %	Name
1	15,11	10151520	50,580	
2	30,52	9918564	49,420	enanti (-)
		20070084	100,000	

Sample Name: AT-101 ODH 9010 1 mL Vial Number: 1

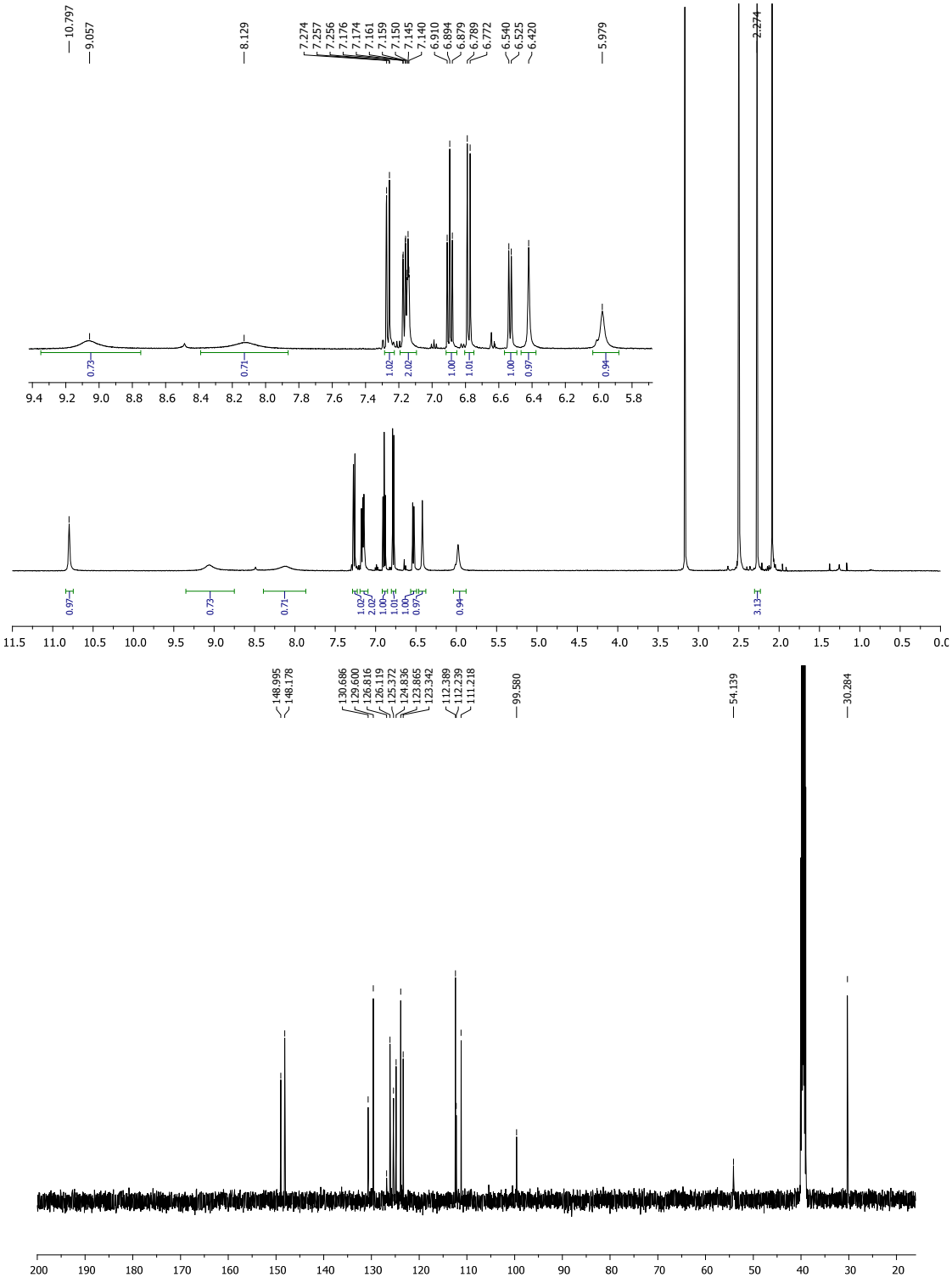


No.	RT	Area	Area %	Name
1	15,08	20059724	91,038	
2	31,01	1974840	8,962	enanti (-)
		22034564	100,000	

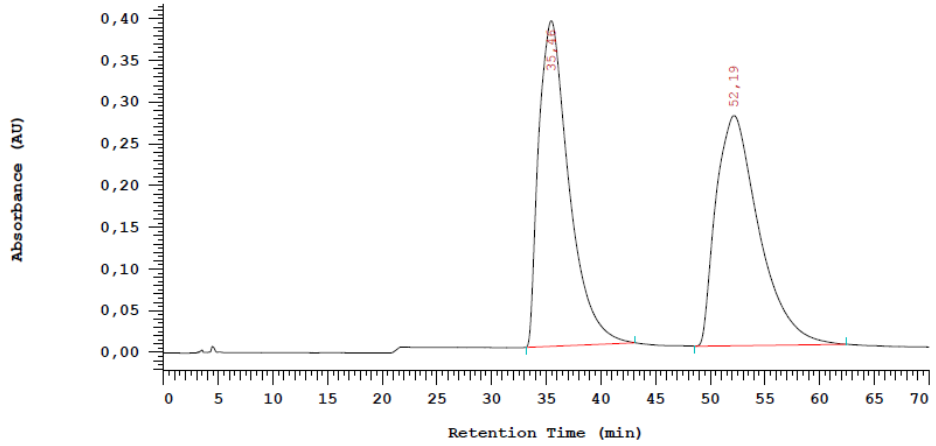
4-(5-Hydroxy-1H-indol-4-yl)-8-methyl-3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (7g)



7g

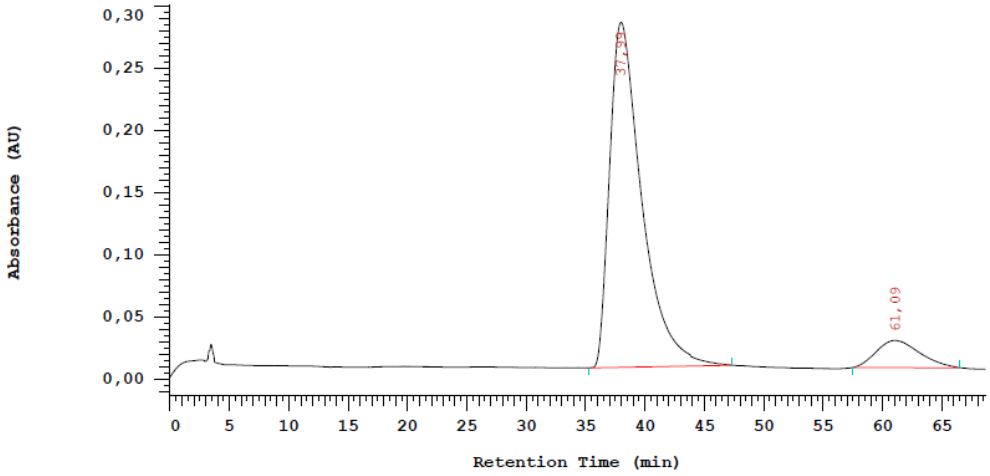


Sample Name: AT-106-27-6 ODH 9010 1 mL Vial Number: 1



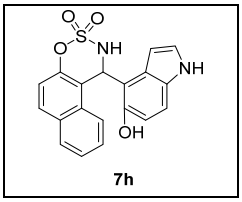
No.	RT	Area	Area %	Name
1	35,46	37353686	49,848	
2	52,19	37581820	50,152	
		74935506	100,000	

Sample Name: AT-106 ODH 9010 1 mL Vial Number: 1

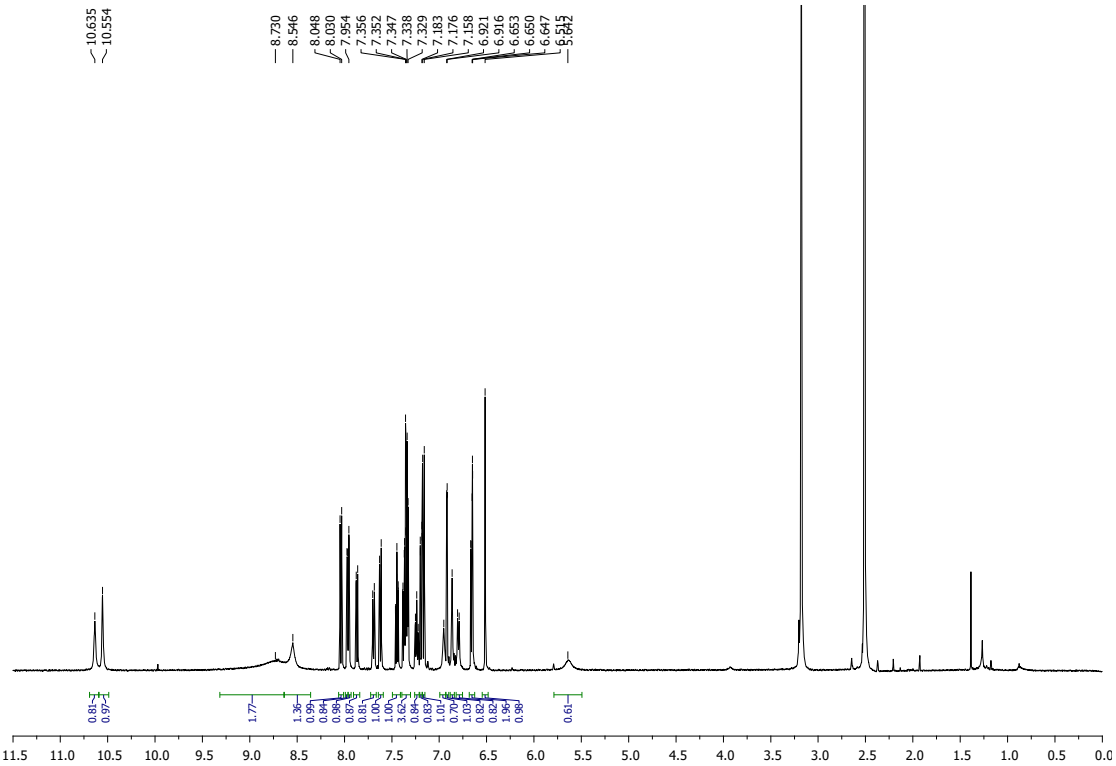


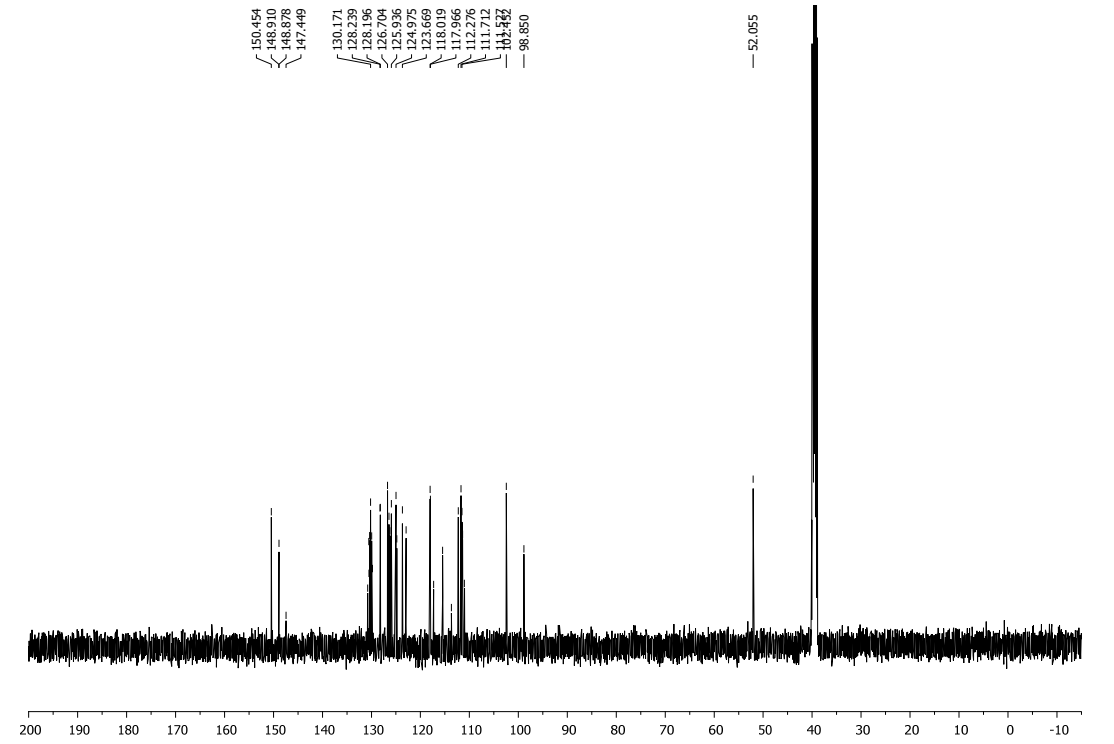
No.	RT	Area	Area %	Name
1	37,99	25990724	90,401	
2	61,09	2759835	9,599	
		28750559	100,000	

1-(5-Hydroxy-1*H*-indol-4-yl)-1,2-dihydronaphtho[1,2-*e*][1,2,3]oxathiazine 3,3-dioxide (7h)

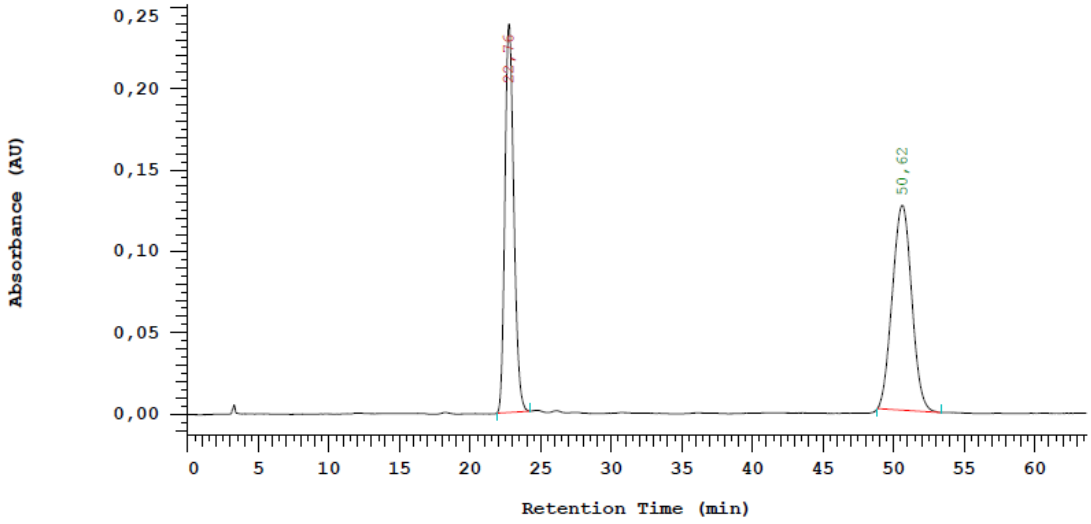


7h



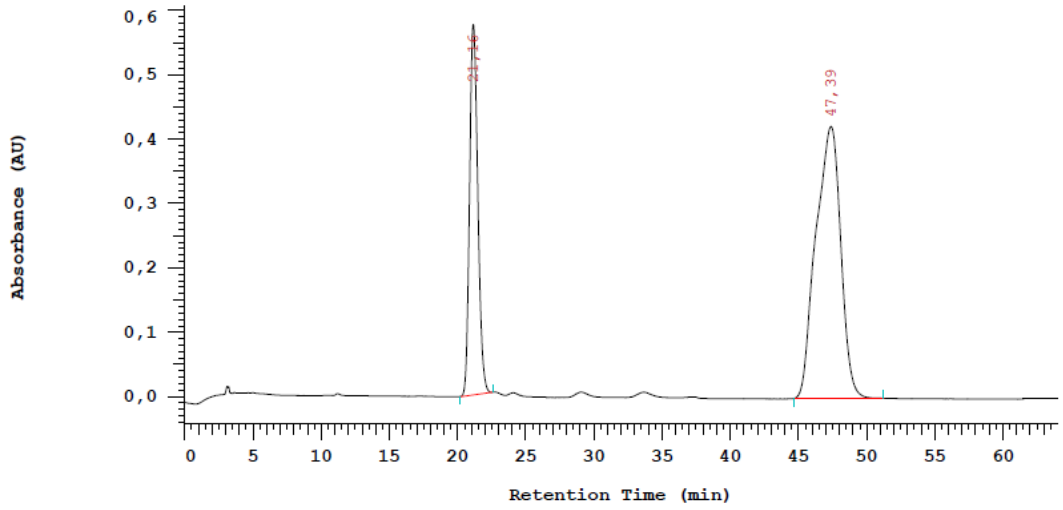


Sample Name: AT-98 ADH 8020 1 mL Vial Number: 1



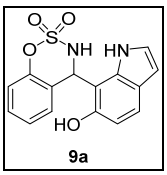
No.	RT	Area	Area %	Name
1	22,76	5125110	46,236	enant. (+)
2	50,62	5959480	53,764	
		11084590	100,000	

Sample Name: AT-100 ADH 8020 1 mL Vial Number: 1

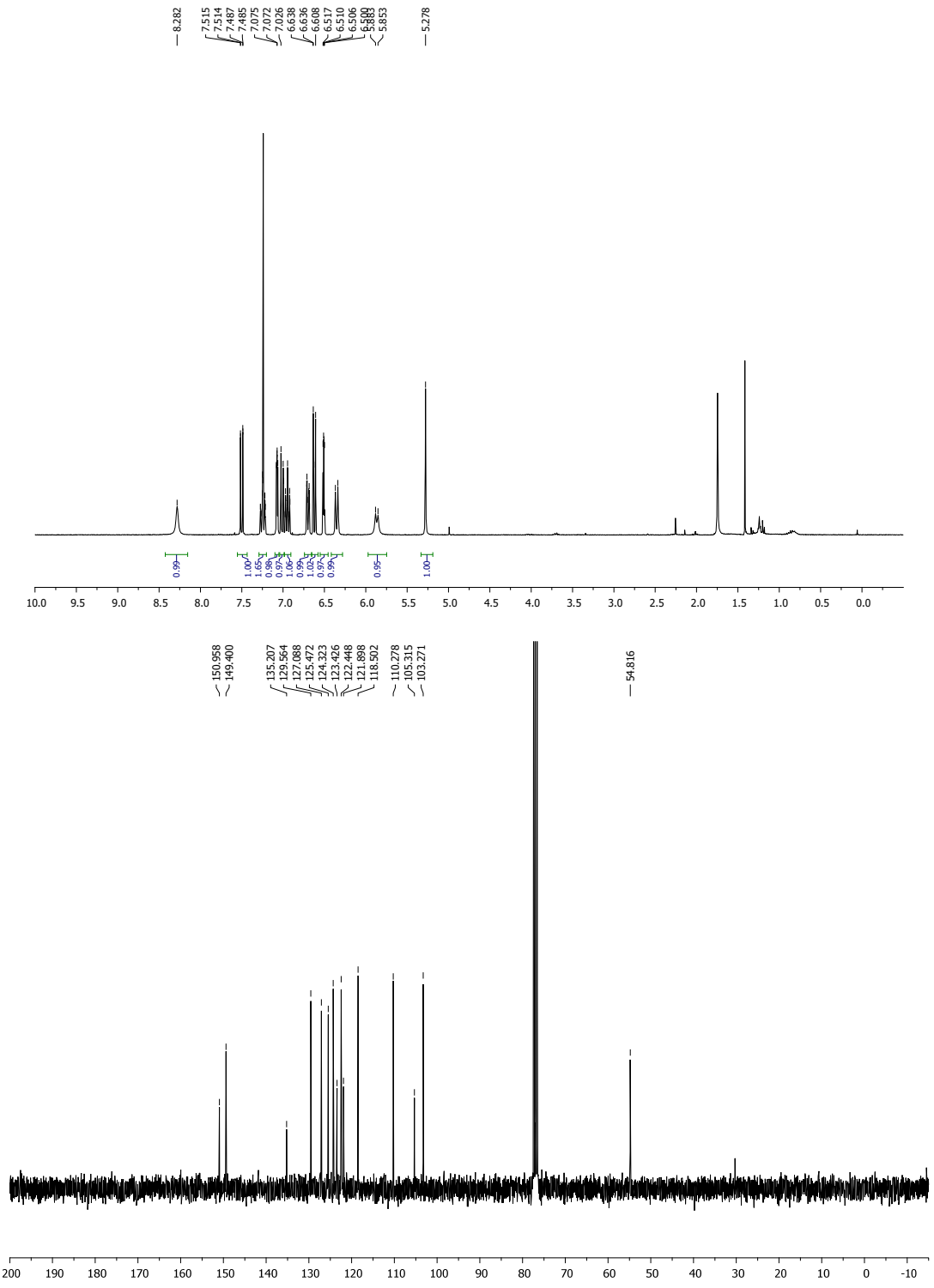


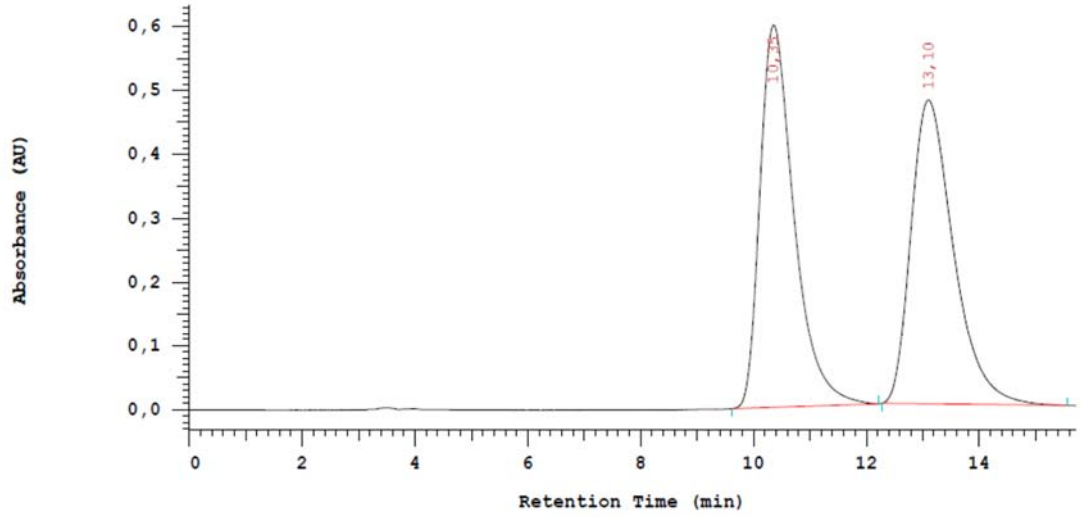
No.	RT	Area	Area %	Name
1	21,16	11989460	31,104	
2	47,39	26557480	68,896	
		38546940	100,000	

4-(6-Hydroxy-1*H*-indol-7-yl)-3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (9a)



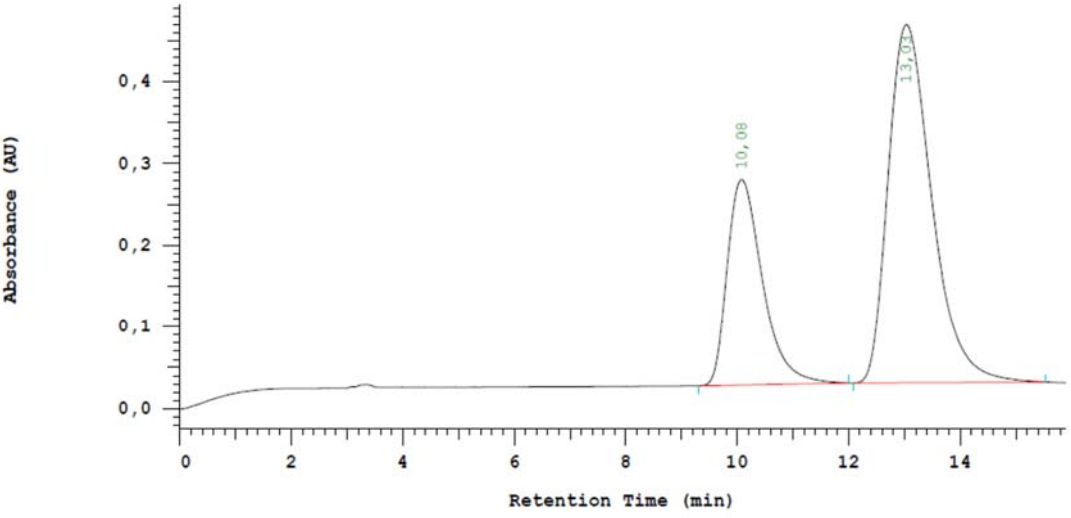
9a





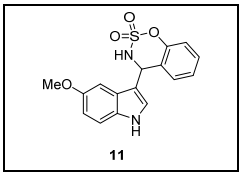
No.	RT	Area	Area %
1	10,35	12571755	50,167
2	13,10	12487915	49,833

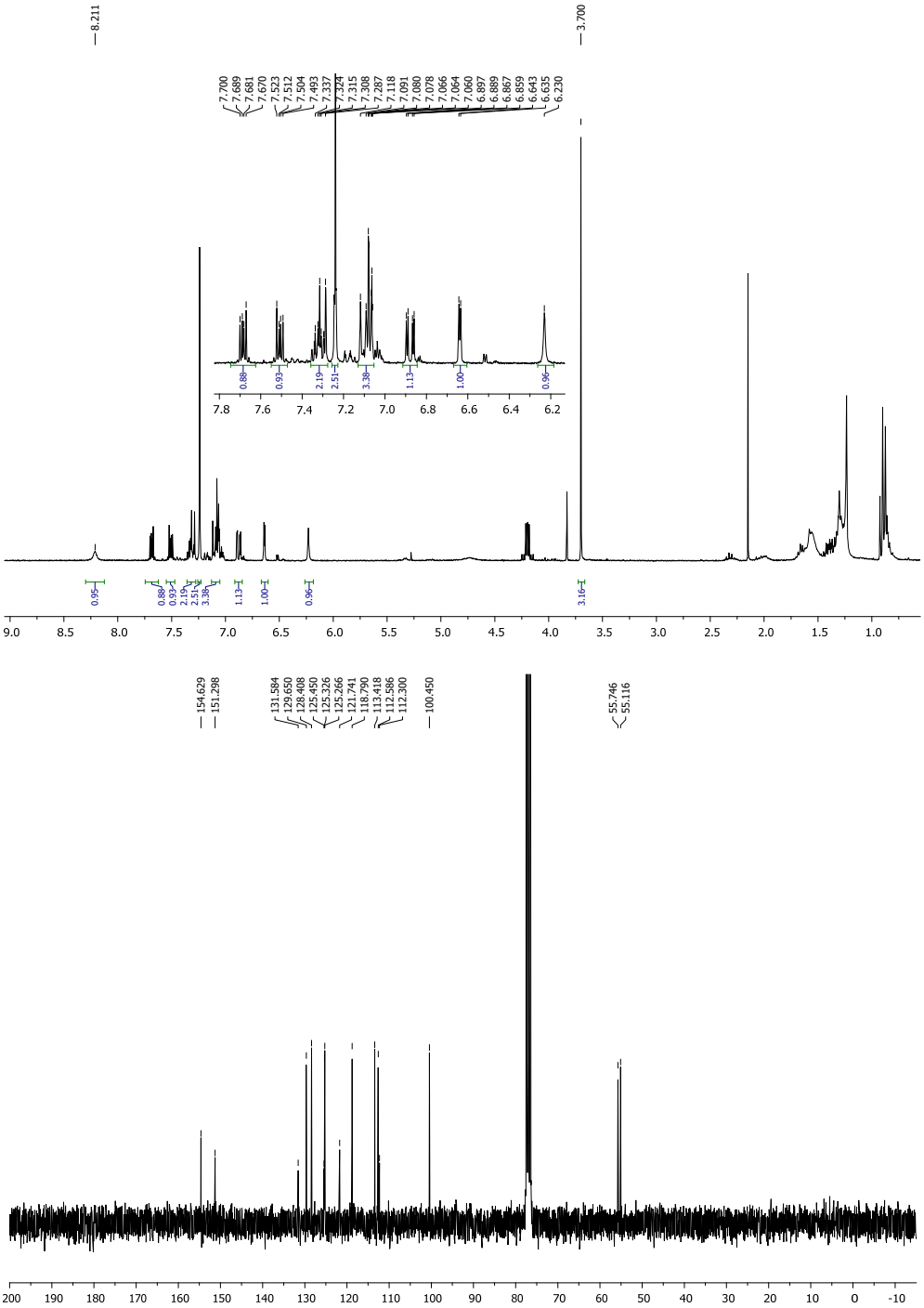
Sample Name: AT-77 ODH 8020 1 mL Vial Number: 1



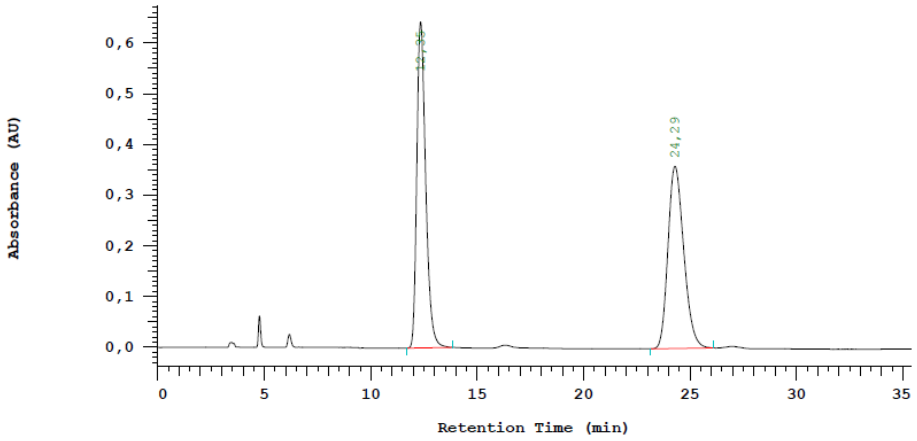
No.	RT	Area	Area %	Nam
1	10,08	5534810	31,699	
2	13,03	11925790	68,301	

4-(5-Methoxy-1*H*-indol-3-yl)-3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (11)



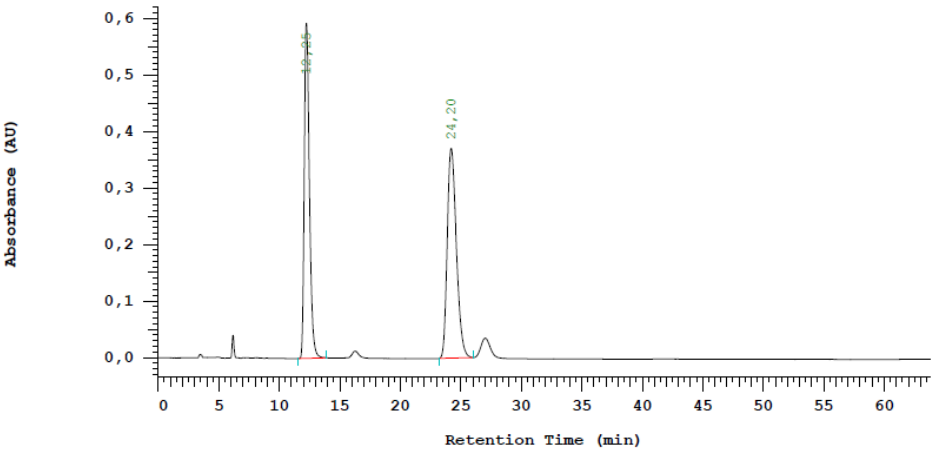


Sample Name: AT-113 IC 8020 1 mL Vial Number: 1



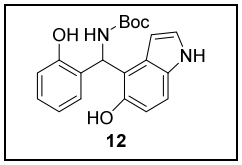
No.	RT	Area	Area %	Name
1	12,35	9204760	50,038	
2	24,29	9190860	49,962	enant. (+)
		18395620	100,000	

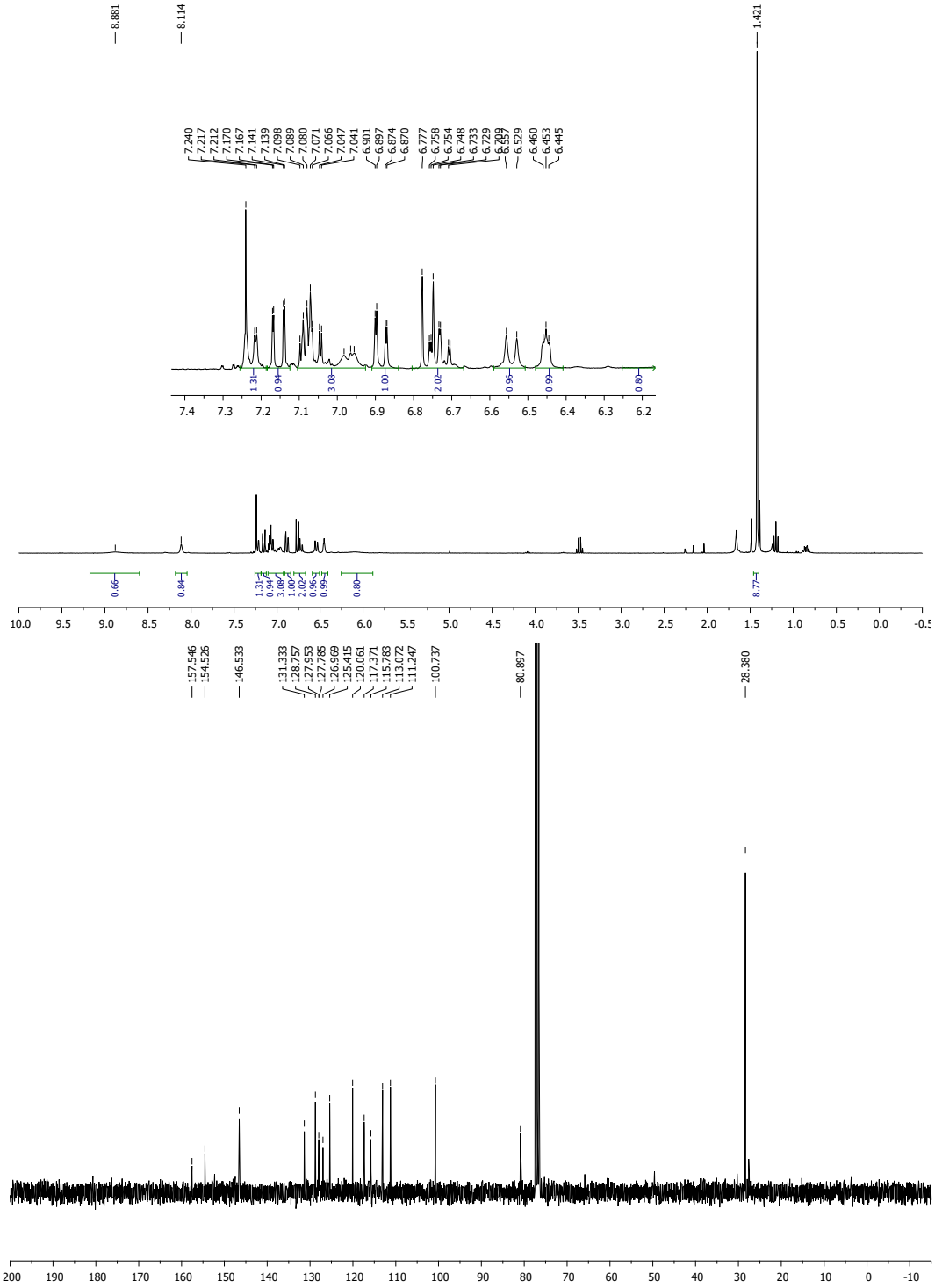
Sample Name: AT-114 IC 8020 1 mL Vial Number: 1



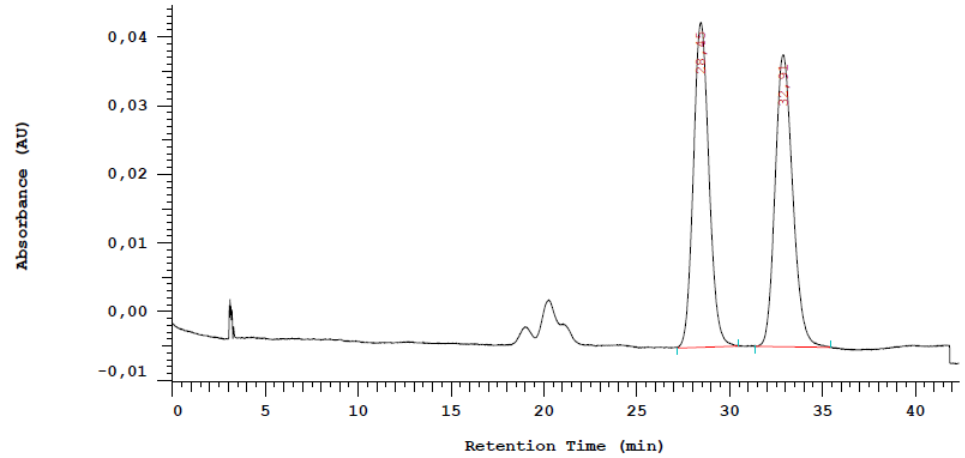
No.	RT	Area	Area %	Name
1	12,25	8497060	46,943	
2	24,20	9603760	53,057	enant. (+)
		18100820	100,000	

***tert*-Butyl ((5-hydroxy-1*H*-indol-4-yl)(2-hydroxyphenyl)methyl)carbamate (12)**



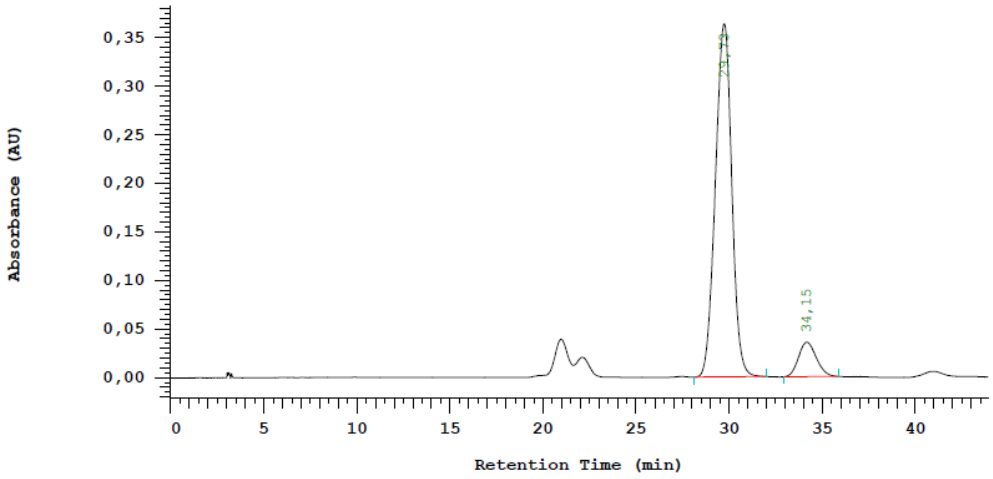


Sample Name: AT-105B ADH 9010 1 mL Vial Number: 1



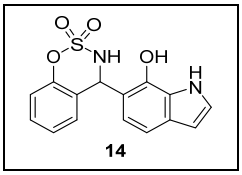
No.	RT	Area	Area %	Name
1	28,45	1377130	49,586	enanti (-)
2	32,91	1400105	50,414	
		2777235	100,000	

Sample Name: AT-111B ADH 9010 1 mL Vial Number: 1

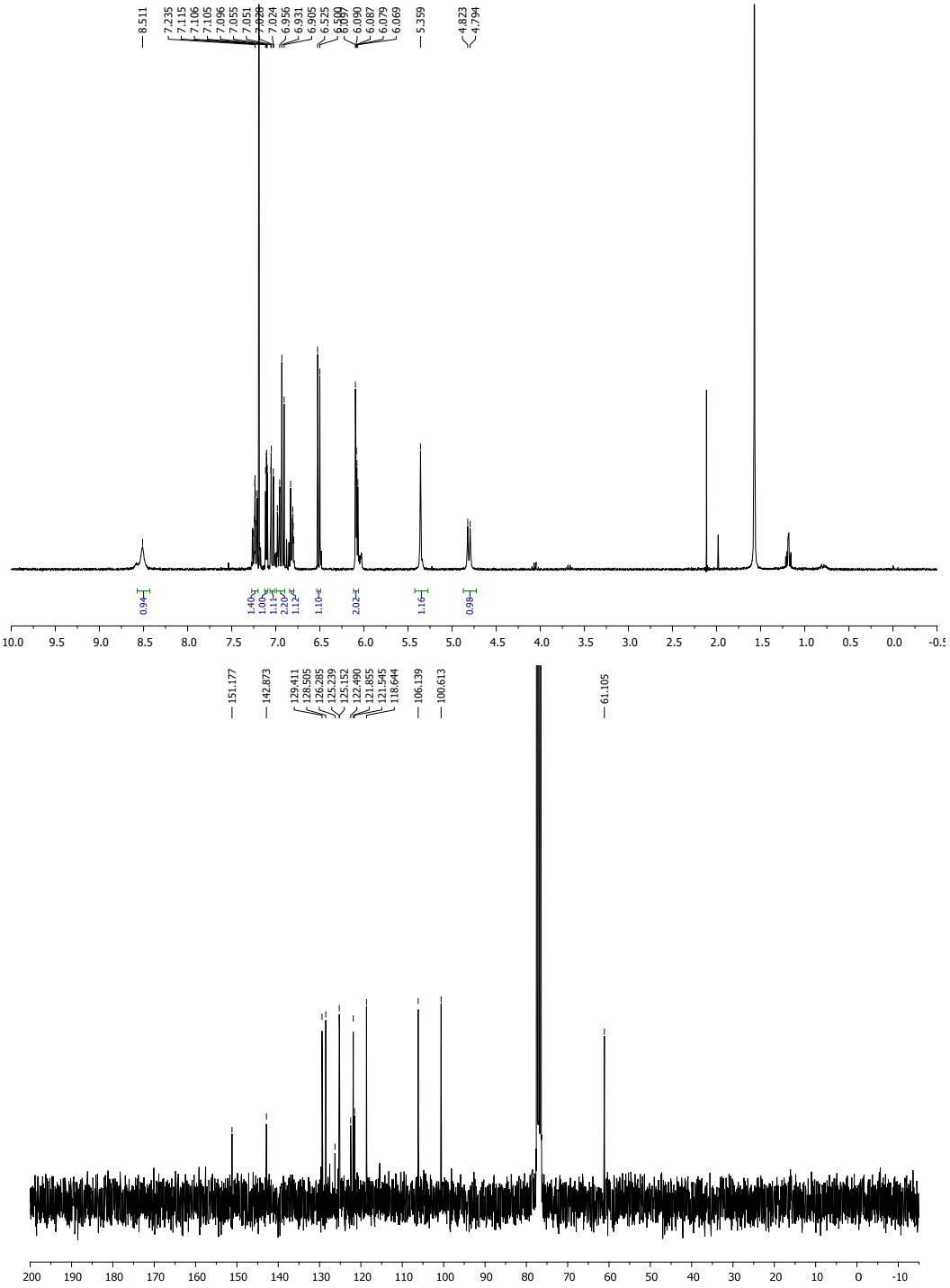


No.	RT	Area	Area %	Name
1	29,73	11061740	90,379	enanti (-)
2	34,15	1177540	9,621	
		12239280	100,000	

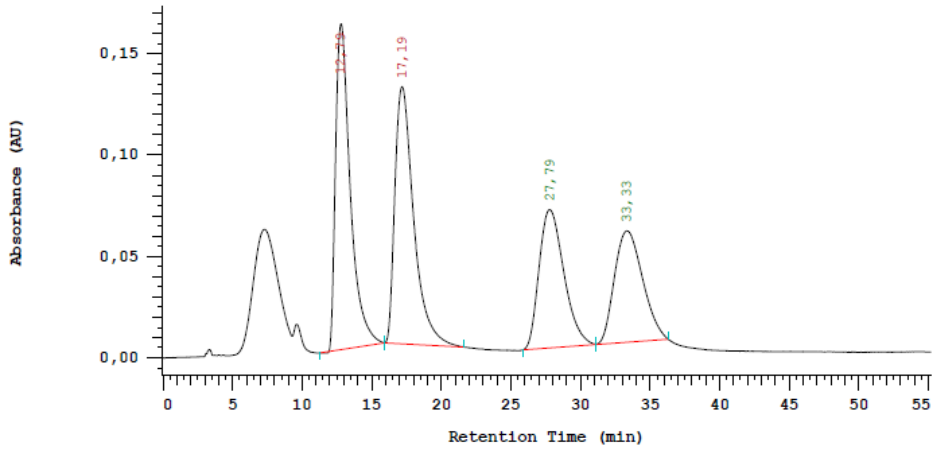
4-(7-Hydroxy-1*H*-indol-6-yl)-3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (14)



14

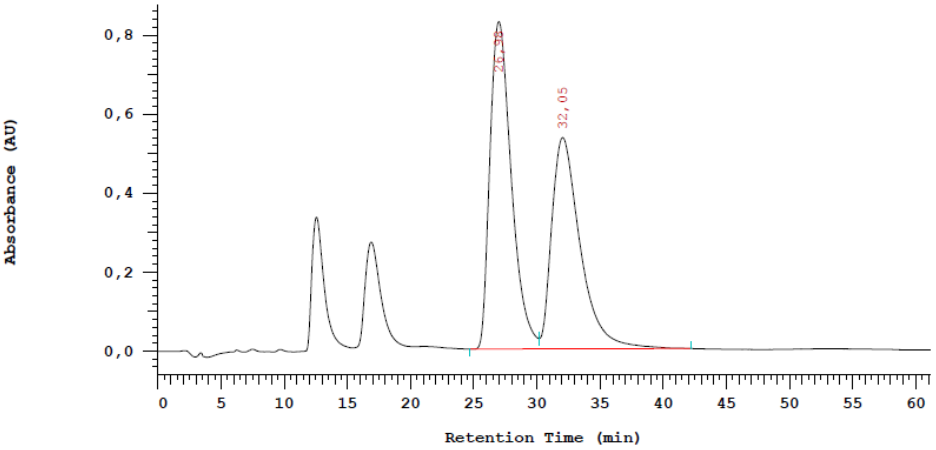


Sample Name: AT-79C ODH 8020 1 mL Vial Number: 1



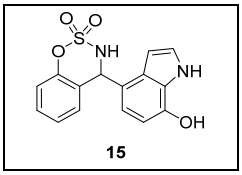
No.	RT	Area	Area %	Name
1	12,79	5845964	29,504	
2	17,19	5912850	29,841	
3	27,79	4210173	21,248	enanti (-)
4	33,33	3845451	19,407	
		19814438	100,000	

Sample Name: AT-83C ODH 8020 1 mL Vial Number: 1

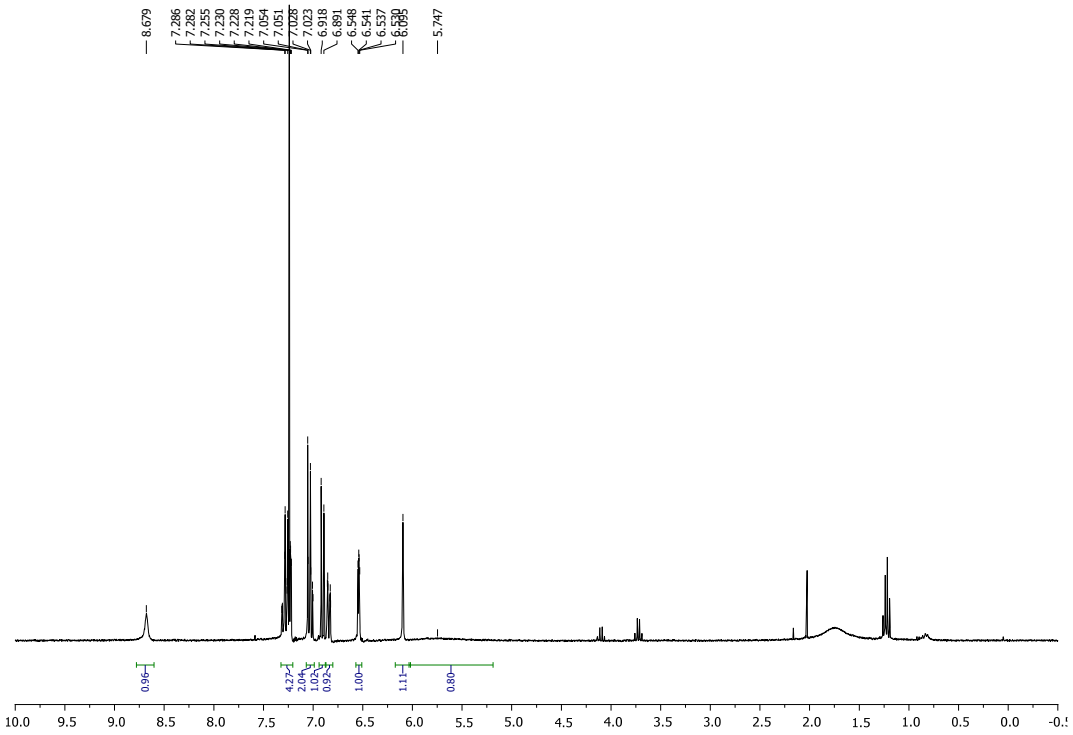


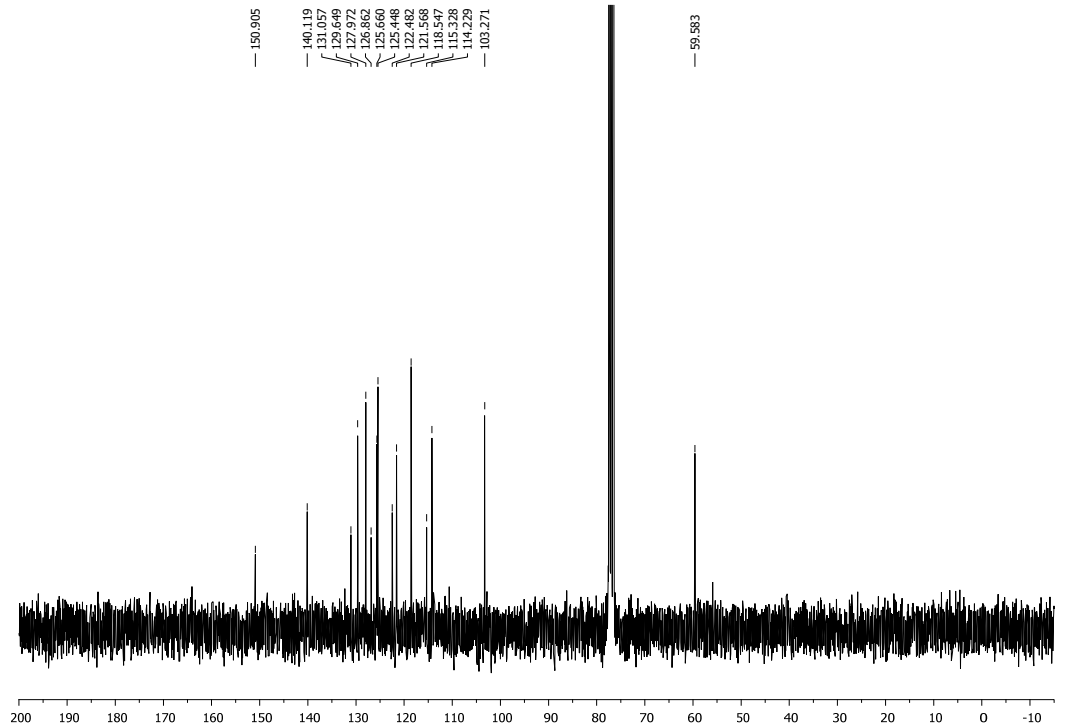
No.	RT	Area	Area %	Name
1	26,98	48754137	53,777	enanti (-)
2	32,05	41905152	46,223	
		90659289	100,000	

4-(7-Hydroxy-1*H*-indol-4-yl)-3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (15)

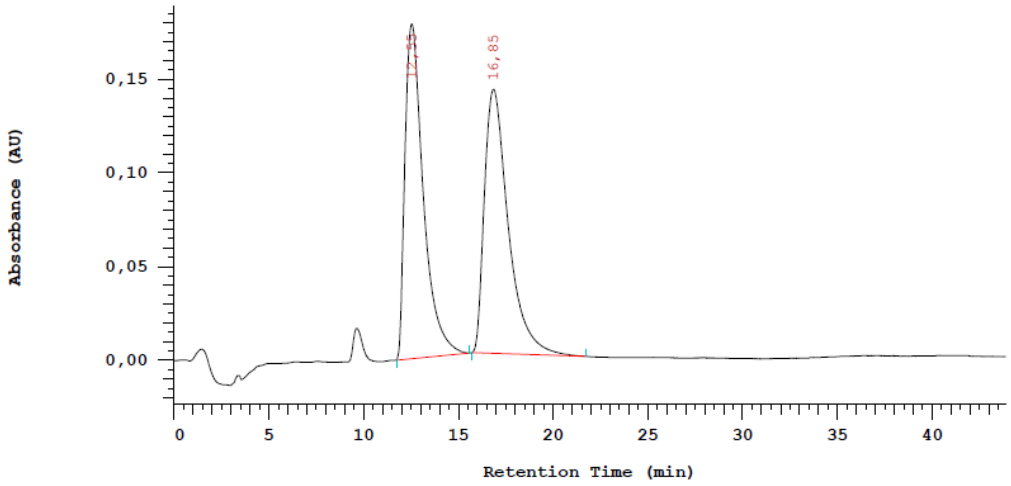


15



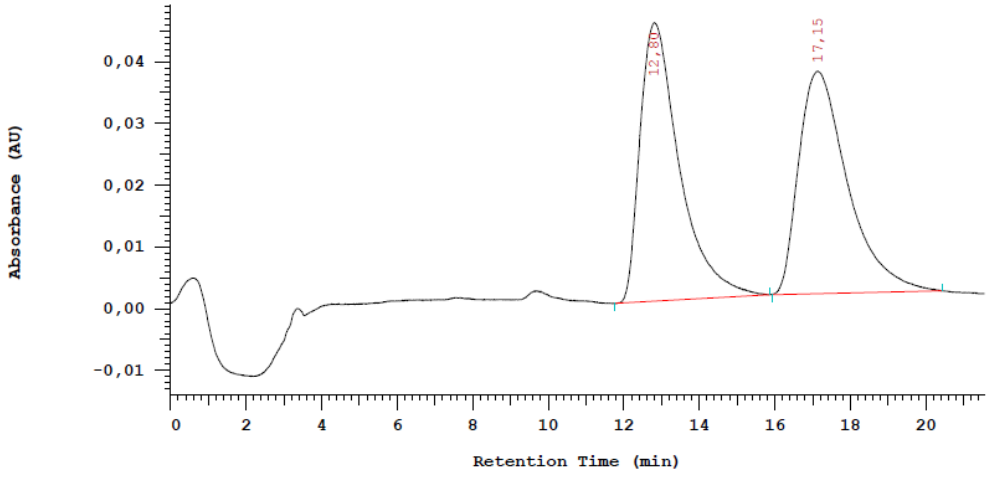


Sample Name: AT-79B ODH 8020 1 mL Vial Number: 1



No.	RT	Area	Area %	Name
1	12,55	5979790	49,233	
2	16,85	6166160	50,767	
		12145950	100,000	

Sample Name: AT-83B ODH 8020 1 mL Vial Number: 1



No.	RT	Area	Area %	Name
1	12,80	1636920	50,247	
2	17,15	1620805	49,753	
		3257725	100,000	